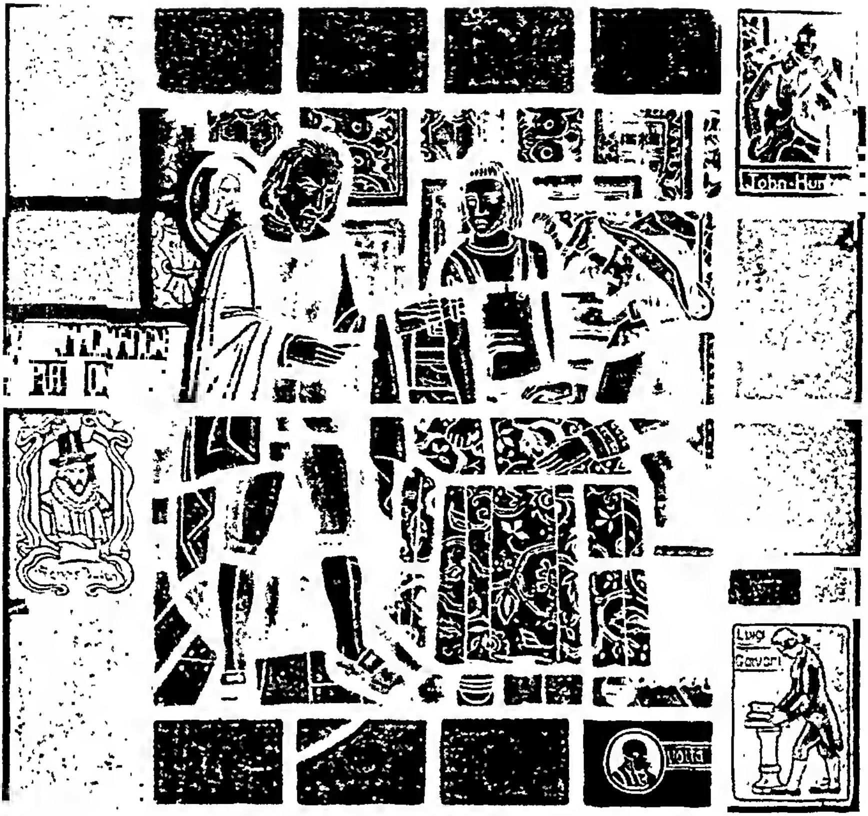

The frontispiece of this book is a photograph of the tenth panel in the stained glass window on the east wall of the Great Hall in the Mayo Foundation House in Rochester, Minnesota, the former home of Dr. and Mrs. W. J. Mayo. It is reproduced here by permission of Dr. Donald C. Balfour, Director of the Mayo Foundation for Medical Education and Research, Graduate School of the University of Minnesota.

This panel, one of twelve which comprise this beautiful window, depicts William Harvey demonstrating the heart and circulatory system to King Charles I. The small blocks forming the border contain likenesses of Francis Bacon, John Hunter, Luigi Galvani and Alessandro Volta. The quotation is from Claude Bernard: "Put off your imagination when you enter the laboratory, but put it on again when you leave."

For a detailed description of the window, the reader is referred to the publication, "A stained glass window on the history of medicine," Bulletin of the Medical Library Association, 32:488–495 (October) 1944, by Dr. Donald C. Balfour and Mr. T. E. Keys.

The historical theme portrayed in this exquisite window is the same theme which has formed the basic philosophy of the Mayo Clinic and the Mayo Foundation from the time of their inception. This comprises the proper integration of medical practice, medical education and medical research.

A History of THE HEART AND THE CIRCULATION

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FOREWORD

MEDICAL HISTORY will probably record the present era as one of such great achievement that it will stand as one of the most significant of all times. There is evidence on every hand that the fundamental discoveries which have been made recently, particularly in respect to preventive medicine, have brought immeasurable benefit to mankind. It is natural, therefore, that in the minds of both the profession and the public, medicine is on the threshold of even greater accomplishments. With these advances toward the better understanding of disease and its prevention and control, it is also true that there are many conditions the cause of which is obscure and the treatment of which is uncertain or at present valueless. Progress goes hand in hand with disclosure of unsolved problems. It is this that makes medicine the most satisfying of all professions and will always attract those who are imbued with the desire to extend its frontiers still farther.

The common factor in achievements in all the phases of medicine, surgery and medical research became apparent during the war, when the urgency of the situation made it obvious that co-ordinated effort and pooling of knowledge were the most effective approach to the solution of any problem. The results of such co-ordinated effort in some of the more recent discoveries in medicine are clear evidence that the utilization of the full power of organized medicine and organized research offers the greatest promise for the elucidation of these problems.

In a systematic approach toward any project to advance knowledge in a field it is axiomatic that intimate knowledge and understanding of the historical data pertaining to the field are essential, for as Winston Churchill has said of history in general, the farther we can look into the past the farther we can look into the future. It is, therefore, unwise to disregard the observations and the interpretations of those observations which the great minds of the past have made. This is particularly true in the field of cardiology, for of all the diseases which afflict mankind, heart disease occupies a place of ever-increasing importance among the medical specialties. It is because of this that a signal contribution to this specialty has been made when clinical investigators with the experience of Dr. Willius and Dr. Dry have assembled the pertinent facts from the work of those physicians and scien-

tists of the past, who with meager facilities for investigating clinical phenomena, nevertheless laid the foundation on which modern cardiology has been based.

For this reason this review of the history of the heart and circulation, aside from being delightful reading, becomes a necessary part of any project that has to do with advancing knowledge of the field of cardiology.

DONALD C. BALFOUR, M.D.

PREFACE

MEDICINE, perhaps more than any other branch of learning, is dependent on and intimately influenced by many essential and interrelated principles. The first principle is, of course, the *science* of medicine, which has its origin in many roots. Proficiency in the science of medicine is a prerequisite in the development of an accomplished physician. The second principle, which is largely the outgrowth of innate endowment and experience, is the *art* of medicine. It comprises such factors as patience, understanding, compassion, tact and other finer sensibilities of humanity. The third principle concerns the *ethics* of medicine and embodies such qualities as honesty, sincerity of purpose and a highly developed professional conduct. Without the possession of a superior ethical sense both the science and the art of medical practice become inadequate. Finally, the *culture* of medicine, a most important yet frequently neglected principle, completes the comprehensive professional personality. These four principles must be so carefully interwoven that a uniform professional texture is created in which one constituent does not predominate at the expense of the others.

During recent years a greater interest in the cultural aspects of medicine has become apparent. A striking example of this is observed in the growing interest and appreciation of the history of medicine and the medical classics. This trend is encouraging because no field of scientific endeavor can truly be said to have attained full maturity while still ignoring its cultural heritage. Rosen* in a recent publication makes the following significant statement: "History is one of the most powerful driving forces in human development. Every situation that man has faced and every problem that he has had to solve have been the product of historical developments and processes."

In undertaking this project dealing with the historical development of knowledge relating to the heart and circulation, we in no measure underestimate our great responsibility in recording events accurately and comprehensively. Our personal interest in the history of medicine over the years had led us to delve extensively into the records of the past, but even having done so we realize that certain important contributions may well have escaped our notice. It is impossible for compilers of medical history to have access to all the original manu-

* Rosen, George: What is past, is prologue. J. Hist. Med. & Allied Sc. 1:3–5 (Jan.) 1946.

scripts and records and they must, therefore, to a certain degree trust the reliability and accuracy of previous writers and professional historians. Thus we are aware of the possibility that certain errors and inaccuracies may be unwillingly and unwittingly perpetuated.

Certain well-qualified scholars of history and literature conscientiously believe that no historical documentation should ever be undertaken unless each and every original record has been carefully studied. If this philosophy had been universally adopted, the literature of the world would contain only fragmentary sequences of historical events. Numerous works dealing with the history of medicine are now in existence and while none of them is without some errors and therefore none of them is scholarly precise according to the aforementioned standards, they nevertheless are of great value and importance. Therefore, the problem of historical documentation rests on two divergent philosophies: the first defending the premise that no documentation is better than one which may contain certain errors; the second that it is desirable to have a documentation of historical data, even admitting that errors will occur because not all original sources are available. The authors of this volume, obviously, are advocates of the second philosophy.

Furthermore, certain critics are of the belief that an undertaking of this type should be preserved for the professional historians and should not be undertaken by physicians. From the standpoint of historical knowledge as it applies to the heart and circulation, the professional historians have been accorded several centuries to fulfill their obligations in this regard but have not as yet produced a comprehensive work. The interpretation of medical data, even those of remote eras, is in reality a function of the physician.

Some modern authors, writing on medical history, have deliberately avoided the ancient eras of medical development with the comment that the early documents contained inaccurate information, that the interpretation of observations was speculative and erroneous and that medical knowledge was so limited as to be valueless. Furthermore, the contention was stressed that ignorance, mysticism, superstitions and various prohibitions rendered the accumulation of such material not only confusing but useless. We decidedly disagree with this philosophy, even admitting certain truths in the criticisms. No record of history is complete without the inclusion of observations and beliefs even though subsequent development proved them to be erroneous. The development of man and of his actions, behavior, processes of thought, beliefs, culture and knowledge represents a metamorphosis, the components of which, correct or fallacious, are integral to the uncompleted fabric which we recognize today as modern medicine.

In the presentation of this material the principles of chronology cannot be avoided without submerging subject matter in inaccessible confusion. We have, therefore, decided to employ the following order which is somewhat arbitrary yet follows the natural cleavages of history: (1) Antiquity, beginning with the first available documents pertaining to the heart and circulation and extending approximately from 3000 B. C. to 1096 A. D.; (2) the Medieval Era, spanning the years from 1096 to 1453; (3) the Renaissance, covering the period from 1453 to 1600; (4) the seventeenth century; (5) the eighteenth century; (6) the first half of the nineteenth century; (7) the second half of the nineteenth century, and (8) the first quarter of the twentieth century.

In order to render material readily accessible, each era is treated chronologically. A general narrative scheme of presentation ignoring chronology would perhaps be read with greater ease but would obviously necessitate considerable repetition to maintain continuity of thought and avoid confusion. The attempt has been made, as each era is discussed, to record the state of existing civilization and to emphasize the advantages as well as the limitations of the period. These comments include the social and political status of the era, customs and beliefs, the influences of religious and other prohibitions, the evolution of mediums for the dissemination of knowledge, and the development of medical teaching.

Biographic comments regarding the individuals included in this work are brief but sufficiently defined to identify them to the reader. In addition, a selected group of contributors, whose works, discoveries and influence have profoundly affected the entire course and development of knowledge of the cardiovascular system and its diseases, are accorded special and more detailed biographic recognition. We realize that some readers may disagree with our selection but it is doubtful whether such a selection could possibly achieve unanimity. These special biographies comprise the second section of the volume.

The third section of the volume is devoted to a modified summary presentation of subject matter. This necessitates some repetition but is deliberately done in order to permit ready reference to the various subjects which, owing to the chronologic method of presentation, occur at random. In each inclusion of this nature reference is made to its appearance in the main text for more detailed information. Direct quotations from the original works appear from time to time. In general these are brief and when translations from another language are recorded we trust that they have been accurately inscribed. We also trust that our interpretation of various early contributions in relation to present-day knowledge and concepts is correct. It is our hope that we have maintained the living union of thought, action and diction.

We wish to express our thanks to our able editor, Dr. John R. Miner, of the Division of Publications of the Mayo Clinic, whose interest in our project and whose many valuable suggestions and criticisms have been of inestimable value. Also we express our sincere appreciation for the splendid co-operation and help so generously accorded us by Mr. Thomas E. Keys and his staff of the Mayo Clinic library. We also extend thanks to our publishers, W. B. Saunders Company, of Philadelphia. Our thanks and appreciation are also extended to other publishers, their editors and authors who have graciously permitted us to republish numerous illustrations.

Owing to the fact that the illustrations in this volume are numerous and many of the likenesses are reproduced on a reduced scale, extensive legends to the illustrations would be cumbersome and impractical. We have, therefore, included a separate list of illustrations recording the many acknowledgments and giving full credit for the permission of republication to each publisher and the respective authors. We are grateful to them for their generous permission.

Our publishers have permitted us to reproduce many illustrations from Garrison's "An Introduction to the History of Medicine" and several illustrations from Allen, Barker and Hines' "Peripheral Vascular Diseases." For these courtesies we again extend our appreciation.

March, 1948 THE AUTHORS

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I

THE CHRONOLOGIC PRESENTATION OF KNOWLEDGE RELATING TO THE HEART AND CIRCULATION

5000 B. C. to 1925 A. D.

ANTIQUITY

*The past lives in us in new forms.**

In tracing the historical development of knowledge relating to the heart and circulation it is necessary to begin the commentary with the first available documentary evidence. Therefore, no attempt will be made to consider the meager data which exist pertaining to the eras of prehistoric man, derived chiefly from skeletal remains and from the crude art of these remote periods, because they are of little significance in this discussion.

THE INFLUENCE OF THE EARLY EGYPTIANS

The first documentary evidence of medical writing was discovered in ancient Egypt. These documents, uncovered through excavations, and now residing in museums and other institutions devoted to the preservation of records of the past, are known as papyri. The term "papyrus" had its origin in the fact that the early writing material produced by the ancient Egyptians was prepared from the fibers of the reed Cyperus papyrus, which grew in great profusion on the banks of the river Nile. This crude but strong fabric was white or ivory colored but, with age, became brown and brittle.

During excavations in Egypt a number of papyri dealing with various subjects have been discovered. Seven of these are known to deal with medical and surgical subjects.

In this commentary interest centers around the Edwin Smith Surgical Papyrus, the Ebers Papyrus and the Brugsch Papyrus. Before considering the relevant contents of these early documents it is appropriate to obtain a general concept, at least, of the status of the civilization and culture of the ancient people who left these records behind them.

Before the origin of the Babylonians, it is presumed, a non-Semitic race existed in the Middle East, in the era between 4000 and 3000 B. C., who originated many of the fundamental principles which formed the basis for subsequent civilization. Among these principles were pictorial writing, astronomy and mathematics. These ancients originated the decimal system of notation, measures and weights, divided the year into twelve months, the week into seven days, the hour into sixty minutes and the minute into sixty seconds. They also divided the circle into 360 degrees. This ancient race originated cuneiform characters reading from left to

* John Macy, The story of the world's literature, 1925, p. 14.

right (the Hebrew and Arabic inscriptions were read from right to left). Architecture, pottery, glass blowing, weaving, carpet making, military tactics and music were also accomplishments of this remote civilization.

Astrology, the ancients' concept of astronomy, was applied to the usual and unusual phases of life, and events and action were superstitiously linked with stars and planets. Wars, famines, epidemics and matters of private and public life were believed to be influenced favorably or adversely, as the case might be, by the equinoxes, eclipses, comets, changes in the moon and stars, and other astronomic and meteorologic circumstances. Much attention was centered on coincidences and certain ones were therefore considered lucky while others were unlucky. These superstitions virtually governed the lives of people and were even utilized by the physicians or priests in the prognosis of disease.

It is thus apparent that these ancients lived their lives under the threat of ever-existent superstitions and mysticisms because the explanations of the common phenomena of nature were not understood. Every act of life was threatened by the unseen and the unknown and there is little wonder that these influences also penetrated their scientific endeavors and observations.

A glimpse at the religious beliefs of these early Egyptians is also necessary in order to understand some of their customs and actions. They were very religious people and believed as the Christians do, that the soul lives after death and that their supreme deity, Osiris, would pass judgment for the deeds or misdeeds performed while on earth. They, however, believed that the souls of the dead returned to the earth to reside again in the body. With this conviction in mind they established methods and means for the preservation of the bodies of the dead and constructed elaborate and massive structures to house the preserved bodies into eternity. These beliefs resulted in the practice of mummification of bodies, the earliest and most ingenious method of preservation known. For the wealthy and such rich notables as the Pharaohs, a very elaborate process of preparation was carried out which often consumed as much as seventy days. The bodies were treated with bitumen (mineral pitch), various spices, gums, native sodium carbonate (natron), honey, and probably other substances. In the elaborate mummification the viscera were removed, similarly treated and placed in jars or, in later dynasties, were replaced in the body. Finally, the prepared body was carefully wrapped with linen fabric, inserted in a fitted case of cedar or a paper-like material and then placed in the sarcophagus. For the poor, only salt or salt together with bitumen was used.

The mummies were then placed in stone tombs, which ranged from small and modest, unimpressive structures to the mighty pyramids of ancient Egypt. The religious beliefs of the ancient Egyptians indicated

the return of the soul and thus comfortable quarters were provided for it. Various objects, great and small, were placed in these tombs, such as jewels, pottery, records such as papyri, food and drink, and even chariots as in the case of the Pharaohs. Thus these ancient customs, while perhaps incomprehensible to the modern mind, served to preserve important evidence reflecting the knowledge, the beliefs and the culture of the times.

These comments are in no way intended to deprecate this magnificent and ancient civilization but rather to enable the reader to understand better the handicaps experienced by the ancient healers and scientists. What may appear to be tragic shortcomings to the modern, are in reality not shortcomings when the limited opportunities of the specific era are understood.

Let the reader further be reminded that the dissemination of knowledge in this era was slow and often unreliable because of the fact that the chief medium of expression was by word of mouth. Only a few—the priests, the scribes and a few scholars—were able to interpret or inscribe the hieroglyphic characters of the language. Before the ingenious Egyptians discovered the method of preparing their papyri for writing material they inscribed their records in stone. This procedure was limited because the process of inscription was slow and laborious and the weight of the stones obviously made them difficult to handle. Somewhat later, the Babylonians inscribed clay bricks and cylinders but even these more portable mediums were cumbersome and limited.

The Phoenicians invented the alphabet but the exact date of this innovation is not known although it is believed to have antedated the birth of Christ by at least 1,000 years. This was a great step forward because writing by means of symbols that represented elementary sounds rather than whole words or syllables was both less tedious and more definite of interpretation than the hieroglyphic characters previously employed. Thus with a paper-like material available and the alphabet invented, the various scripts followed in natural sequence and the art and science of writing became established. It was still, nevertheless, a slow and laborious process within the interpretation of relatively few persons. Texts were few and very expensive to secure.

Still later, other writing materials appeared, parchment or vellum, thin leather skins, which were frequently used as rolls or scrolls and inscribed on both surfaces. Paper, which was invented by the Chinese, was in common use by the fourteenth century, although even then it was produced only in limited quantities.

Thus whole races, even though they were eager to acquire knowledge, were greatly limited because only a select few could read or inscribe and memory for the spoken word is often not long or accurate. Further-

more, even as today, oral repetition is likely to be altered by the prejudice or individual viewpoint of the speaker. Not until books became available to the masses did a common and practical medium of education and enlightenment appear. This important phase of education with special reference to medical knowledge will be considered further as the subsequent eras are reached.

The Edwin Smith Surgical Papyrus. The Edwin Smith Surgical Papyrus is designated by most historians as the most important and revealing document on Egyptian medicine yet discovered. Edwin Smith (1822–1906), America's first Egyptologist, acquired it in Thebes in 1862 and after his death the papyrus was presented to the New York Historical Society by his daughter. The papyrus remained in obscurity for many years but in 1920, the New York Historical Society invited J. H. Breasted, of the Oriental Institute of the University of Chicago, to decipher and translate it. The papyrus dealt with both surgical and medical subjects.

Breasted stated that the Smith Papyrus dates from the seventeenth century B. C., although the author's original manuscript was produced at least 1,000 years earlier, during the Pyramid Age (3000–2500 B. C.). He suggested that the earliest known physician, Imhotep, may have been its author. It is of interest that Breasted dedicated his important work to William Harvey.* Breasted suggested that the papyrus may have been circulated as a book during the time when the great Pyramid of Gizeh was being erected (thirtieth century B. C.). He further suggested that the true title of the Edwin Smith Surgical Papyrus may have been "The secret book of the physician." His reason for this assumption is the appearance of an isolated passage alluded to also in the Ebers Papyrus which was inscribed some fifteen hundred years later. The reference intimates some knowledge of the heart and its movements and the fact that vessels from the heart reach to all portions of the body. Since the identical passage occurs in the Edwin Smith Surgical Papyrus it tends to establish it as original in this ancient document.

The unknown author clearly recognized the heart as the center of a system of distributing vessels but did not of course possess the concept of the circulation of the blood. He also knew of the pulse and is believed to have counted it. This presumption is strengthened by the fact that the first timing mechanism, the water clock, was already in existence and was a product of early Egyptian ingenuity. This ancient physician associated the pulse with the beat of the heart and used this method of examination to determine the action of the heart. He recognized the fact that the pulse is produced by the force and the action of the heart.

* "To the memory of William Harvey discoverer of the circulation of the blood at the three hundredth anniversary of his great discovery this publication of the earliest known surgical treatise is dedicated."

Much later, the early Greek physicians held the belief that an inherent force in the arteries causes the pulse.

It is appropriate to reproduce Breasted's translation of that portion of the Edwin Smith Surgical Papyrus dealing with the pulse wherein the ancient physician orders the method whereby a patient should be examined.*

> As for: "Thou examinest a man," [it means] counting any one – – [⌈like cou]nting⌉ things with a bushel. (For) examining (*ḫ'·t*, literally "measuring") is [⌈like⌉] one's [⌈counting⌉] a certain quantity with a bushel, (or) counting something with the fingers, in order to [know] – – –. It is measuring (*ḫ'·t*) things with a bushel which – – – one in whom an ailment is [cou]nted, like measuring (*ḫ'·t*) the ailment of a man; [in order to know the action] of the heart. There are canals (or vessels, *mt*) in it (the heart) to [every] member. Now if the priests of Sekhmet or any physician put his hands (or) his fingers [upon the head, upon the back of the] head, upon the two hands, upon the pulse, upon the two feet, [he] measures (*ḫ'y*) [to] the heart, because its vessels are in the back of the head and in the pulse; and because its [pulsation is in] every vessel of every member. He says "measure" (*ḫ'·t*) regarding his [⌈wound⌉] because of the vessels (*mt·w*) to his head and to the back of his head and to his two feet – – – – his heart in order to recognize the indications which have arisen therein; meaning [⌈to meas]ure it⌉ in order to know what is befalling therein.

This ancient physician in his discussion of the thorax made no mention of its contents except to call attention to the presence of two vessels, one leading to the heart and the other to the lungs. The papyrus further lists twenty-two vessels distributed to various parts of the body such as the loins, neck, arms, back of the head, forehead, eyes, eyebrows and ears.

The Ebers Papyrus. Another Egyptian papyrus identified as dating approximately to 1550 B. C. is known as the Ebers Papyrus. It was acquired by Georg Ebers at Thebes in the winter of 1872–73. He secured the manuscript from a resident of that city and was informed that it had been recovered from a grave at El Assassif near Thebes fourteen years before. The finder of the document had died and the precise date of the grave and information regarding the identity of the mummy were not available. This papyrus, according to Finlayson, was very difficult to decipher and translate, the translation having been made by H. Joachim in the German language. The papyrus is now at the University of Leipzig. The author of the manuscript is not known. As already noted, the heart and its movements were referred to and comments were

* Breasted used the following typographic signs in his translation: ⌈ ⌉, enclosing a word or words, indicates that everything so enclosed is of uncertain translation. [ ] indicates that words so enclosed were restored by Breasted and that he regarded the restoration as probably correct. [⌈ ⌉] indicates a restoration which Breasted regarded as uncertain. Short dashes mean the loss of words, whose possible but not certain number is indicated by the number of dashes. ( ) indicates that a word or words so enclosed are Breasted's interpretations, not the restoration of a loss in the original text. ' indicates a sound like the initial breathing represented by the unpronounced *h* in "humble."

made that vessels from the heart reach to all portions of the body. In addition to the twenty-two vessels enumerated in the Edwin Smith Surgical Papyrus this manuscript listed fifty more supplying the following parts in various numbers: the nostrils, temples, crown of the head, ears, shoulders, arms, legs, testicles, kidneys, liver, lungs, spleen, bladder, and anus. The text of the papyrus reiterated the belief that the heart is the origin of the vessels which are distributed to all parts of the body.

The ancient Egyptians had a splendid opportunity of observing the interior of the body because their custom of preserving the bodies of their dead necessitated the opening of the body cavities for special treatment of the essential viscera. However, this process was governed by religious provisions, a fact which was perhaps a limiting force in accurate and complete observation.

The enumerations in the Ebers Papyrus clearly indicate that its author had at least a gross anatomic concept of the heart and its vascular tributaries. However, the text demonstrated the influence of superstition and mysticism when the author stated that each ear had two vessels; those on the right side were believed to convey the vital spirit of life while those on the left side were believed to convey the breath of death.

The Brugsch Papyrus. Still another Egyptian papyrus, known as the Brugsch or Greater Berlin Papyrus, was judged to have been inscribed about two centuries after the Ebers Papyrus, sometime in the fourteenth century B. C. It came into the possession of Henri Brugsch and is believed to be the first papyrus discovered. The discovery of this papyrus was described by a Mr. Passalacqua of Paris in his catalogue of books as follows: "It was carefully covered up in a vase of baked clay, along with the small manuscript 1,559 in similar hieratic writing, and bearing a date and *cartouches;* this vase was discovered alone amongst the ruins, at a depth of about ten feet, near the pyramids of Sakarah at Memphis." It is believed to have belonged to the medical library at Memphis and is considered to be the papyrus referred to by Galen in his writings many years later.

Castiglioni dated the papyrus in the reign of Casti, the fifth king of the first dynasty. He commented that the anatomy of the veins was mentioned. Finlayson stated that the references to the heart in this document are similar to those found in the Ebers Papyrus.

Comment. These early medical documents are of significant importance and interest and certainly merit inclusion in any commentary on the history of medicine, even though they are products of inaccurate observation and erroneous speculation. The identity of the authors is not known. As already mentioned, Breasted suggested that Imhotep, the first known physician and architect of the Pyramid Age, may have been the author of the Edwin Smith Surgical Papyrus. In the Ebers

Papyrus, the name Nebseχt appears, designated as "physician, priest, and Lord of healing." Evidently, the writer or copyist of the manuscript was quoting the beliefs and teachings of Nebseχt. However, accounts of the Brugsch Papyrus make no inferences regarding the authorship.

We thus learn from ancient Egyptian medical records that the heart was recognized as a central organ from which vessels were distributed to various parts of the body, including the viscera. The pulse was recognized and counted and the information gleaned from this method of examination was employed to evaluate the status of the heart. Finally, the anatomy of the veins had been investigated. These observations, while relatively meager in terms of present-day concepts, were nevertheless of great importance in laying the cornerstone for subsequent scientific inquisitiveness and adventure.

THE INFLUENCE OF THE EARLY CHINESE

Further medical records of antiquity are found in Chinese medicine, embracing the period of 1123 to 265 B. C. and later. Many of the observations were made during the Chow Dynasty in the age of Lao-tse, Confucius and Mencius. Chinese medicine is believed to have had its origin about 2700 B. C. Its origin, according to legend, is attributable to the Emperor Shen Nung, who taught his people the fundamentals of growing plants and the use of implements for their cultivation. He was said to have compiled an herbal (an ancient book of herbal remedies) containing more than a hundred items. However, progress made in this period and for many subsequent centuries became obscured and forgotten when a complete retrogression in thought and development occurred about 1000 A. D. Pantheism flourished and, as in the case of other races, the deterring influences of mysticism and the occult throttled the progress and development of medicine, sciences, literature and the arts. The principal medical work of that era was the Nan Ching, a text dealing with the arterial and visceral systems which recorded the weights of various organs including the heart. A physician, Pien Ch'iao, who lived during the sixth and fifth centuries B. C., is believed to have been the originator of Chinese pulse lore.

The early concepts of anatomy and physiology were dominated and distorted by mysticism and speculation. Magic and demonic influences pervaded the attempts at scientific conjecture. It was believed that the human body was composed of five principal organs: the heart, lungs, kidneys, liver and spleen. They were thought to exert a controlling influence on the small bowel, colon, gallbladder and stomach. Each principal organ was presumed to correspond to some existing substance or event in nature such as an element, a plant, a color or a season. This concept was similar to the Doctrine of Signatures which was popular in the fifteenth and sixteenth centuries.

Probably the most important work attributed to Hippocrates is the famous "Aphorisms," which is composed of terse generalizations, many of them expressed in the words of proverbs, and some of them confirmed by the clinical experiences of succeeding ages.

Hippocrates advocated and practiced the utilization of mental concentration and analysis together with the application of the five senses in the diagnosis of disease. This doctrine is unmistakably the early formulation of what was later to be known as physical diagnosis. By virtue of his inherent sense of honesty, Hippocrates fully realized the great responsibilities of the physician and was the first to tabulate a high standard of ethics, designed to protect the patient as well as to maintain a high level of dignity for the physician. The Hippocratic Oath of medical ethics undoubtedly expresses his beliefs although it is probable that it was written by someone else.

According to Hippocratic doctrines the heart was not believed to be subject to disease owing to its massive and compact composition. In an anatomic treatise on the heart (circa 400 B. C.) were included descriptions of the cardiac valves, the ventricles and the great vessels. The altered facies of disease (Hippocratic facies) was described and the pulse counted. Hippocrates erroneously held the belief that the arteries were filled with air while the veins contained blood. This belief was widespread among the ancients and is undoubtedly based on the fact that the arteries are empty after death.

Among the "Aphorisms" are certain interesting comments regarding the heart. In one of them is the statement that sudden death is more likely to occur in very obese persons than in thin individuals. In another aphorism, according to Singer, that disturbance in breathing later to be known as Cheyne-Stokes respiration was described. Describing the illness of a patient it is stated that the breathing was like a person recollecting himself, and was large and rare.

Aegimius, a contemporary of Hippocrates regarding whom very little is known, was said by Galen to have written a work on cardiac palpitation. This work included a discussion of the movements of the arteries and undoubtedly referred to the pulse.

Aristotle (384–322 B. C.), also a contemporary of Hippocrates, helped to perpetuate the latter's precepts. Aristotle, a noted philosopher in his own right, was born in Stagira of Asclepiad stock and was a student of the celebrated Plato. His greatest contributions were in the field of biology, and notably in zoology, and little doubt exists that the science of comparative anatomy found its origin in his work. Aristotle named the aorta and declared the doctrine indicating primacy of the heart as the seat of "innate heat." He believed that the number of ventricles in the heart varied with the size of the animal. His observations on the chick embryo probably constituted the first studies in embryology. In

studying the chick embryo on its development day by day, he called attention to the punctum saliens, the fetal heart beat, and noted the vitelline and allantoic veins.

Singer stated that Aristotle did not dissect the human body but carried out extensive dissections in animals. He gave a fairly accurate description of the branches of the great veins and superficial vessels in the forelimb of mammals. Aristotle conceived the brain to be a mechanism for cooling the heart and preventing it from becoming overheated. He also believed the heart to be the first organ to live and the last to die.

Praxagoras (circa 340 B. C.) of Cos, a student of the eminent Diocles, was a disciple of the school of Dogmatists. Among his comments was the observation that the beat of the heart and the pulse were synchronous. The same observation, however, had been suggested by the author of the Edwin Smith Surgical Papyrus some twenty-five centuries earlier.

Herophilus (circa 300 B. C.) of Alexandria, a student of Praxagoras and a leading anatomist of his time, also made observations regarding the heart, vessels and pulse. He is generally credited as being the first to count the pulse, although as already emphasized, certain passages in the Edwin Smith Surgical Papyrus cast doubt on this allegation. Records indicate that he dissected cadavers and acquired practical experience in gross anatomy. Herophilus described the pulmonary artery, which he designated as the arterial vein. He also counted the pulse by means of a water clock, commented on the systolic and diastolic phases of its movements and taught that the pulse had four cardinal properties: frequency, rhythm, size and strength. According to Galen, Herophilus was the first to describe a peculiar pulse called the "*pulsus caprizans*," consisting of an initial stroke believed to result from only partial dilatation of the artery, immediately followed by a more forcible one. It was likened to the leap of a goat. It is possible that Herophilus had observed the extrasystole. Like his contemporaries, Herophilus believed that the arteries were filled with air.

Erasistratus (circa 310–250 B. C.), a contemporary of Herophilus, was one of Alexandria's most famous physicians and teachers. He was of the Cnidian school of medical philosophy. Erasistratus is believed to have been the first to delve into pathologic anatomy when he searched for clues pertaining to the causes of pleuritis and pericarditis. Castiglioni designated him as a physiologist and pathologist rather than an anatomist. Erasistratus described the aortic and pulmonary valves and the chordae tendineae. A most interesting and important belief advanced by Erasistratus and based on reasoning, was his contention that the blood passed from the veins to the arteries by means of small communicating vessels. While he was in error in reversing the true direction

of the peripheral circulation he nevertheless reasoned correctly regarding the necessity for the existence of vascular anastomoses. He thus contended that the arteries contained blood and not air, he predicted the existence of the capillary circulation, which was not demonstrated until 1661, and he was on the threshold of conceiving the circulation of the blood. According to him, the chief cause of disease was plethora (hyperemia), on the basis of which he explained angina (sore throat), pleurisy and dropsy. He also described the valves of the veins.

THE INFLUENCE OF THE EARLY ITALIANS

While Roman civilization and culture were growing in this part of the era, Greece had made remarkably greater progress and had unmistakably developed the pattern for that period of history. Even in spite of other accomplishments, Roman medicine was virtually nonexistent. Whatever counterpart of the healing art existed was based on magic and superstition. The multitude of synthetic deities who dominated the very existence of these ancient Romans were called on to bring about cures. Even the geographic proximity of Italy and Greece did not afford the opportunity for the exchange of ideas and knowledge. Cato (234–149 B. C.), a powerful figure in his time, held a great distaste for all physicians, and Greek physicians in particular. He was imbued with the obsession that the Greeks deliberately intended to poison their patients and that they considered the Romans to be barbarians. Gradually, however, Greek physicians came, practiced and taught their science and in time won the confidence of the Romans. One of the first Greek physicians to practice medicine in Italy was Archagathus of the Peloponnesus, who came to Rome in 219 B. C. Asclepiades of Prusa, born about 124 B. C., known as the prince of physicians, wrought an important influence on the acceptance of Greek medicine and frequently acted as consultant to foreign monarchs and to prominent and wealthy Roman families.

Roman medicine made little or no progress until the reign of the Caesars (Caius Julius [100–44 B. C.], Octavian and his adopted son. Tiberius [42 B. C.–37 A. D.]). It was not until the time of Aurelius (Aulus) Cornelius Celsus, who lived during the early part of the first century, that genuine medical progress became evident.

Aurelius (Aulus) Cornelius Celsus was one of the most colorful personalities of the early Roman Empire. Apparently not a physician but an encyclopedist, he attempted to gather and record all available knowledge regarding various phases of many sciences. His famous work, "De re medicina," was printed many years later (1478) in Florence. The first account of heart disease recorded in Latin is credited to Celsus. He discussed the disease which the Greeks called "kardiakon" and insisted that it represented only excessive weakness of the body due to profuse

sweating and that associated with this was a slow and weak pulsation of the arteries. For its treatment, Celsus recommended the application of astringent poultices to the precordium, measures not mentioned to prevent sweating, small quantities of food and wine at frequent intervals and the use of nutrient enemas if necessary.

Lucius Annaeus Seneca (4 B. C.–65 A. D.), the Roman stoic philosopher and author and not a physician, described the symptoms of his own disease and unknowingly recorded the earliest description of the anginal syndrome of coronary insufficiency. The description was found in his fifty-fifth epistle and was discovered many years after his death (1529). The vivid description was inscribed as follows: "The attack is very short, and like a storm. It usually ends within an hour. . . . To have any other malady is only to be sick, to have this is to be dying."

Aurelius (Aulus) Cornelius Celsus.

Rufus of Ephesus, who lived in the reign of Trajan (98–117 A. D.), was a disciple of the early Roman schools of pneumatic and eclectic medicine. He contributed a work on anatomy and several treatises on the pulse wherein he stated that the pulse, heart beat and systole were synchronous events. According to Horine, it is possible that Rufus also described the carotid sinus reflex. In his work he mentioned the observation that when the arteries of the neck of an animal were firmly pressed, the animal became drowsy and lost voice. Rufus was of the opinion that these phenomena did not occur from pressure on the vessels but rather from pressure on the contiguous nerves. In his observations of the pulse he noted its size, frequency, strength and resistance and recognized the fact that the movements of the fontanels in infants were produced by arterial pulsations.

Archigenes (circa 54–117 A. D.) of Apamea was a Greek by birth but practiced medicine in Rome. Like Rufus, he proclaimed the doctrines of the pneumatic school of medicine. He wrote about the pulse and his belief centered about the tenets of "*pneuma*." *Pneuma* was considered to be the basis of health and with *pneuma* in balance, tonus was maintained which in turn could be detected by the pulse. Each pulse beat was said to consist of four phases: contraction, dilatation, and two periods of rest.

THE INFLUENCE OF OTHER ANCIENTS WITHOUT REGARD TO GEOGRAPHIC PARTITION

Owing to the basic intention to present the text in a chronologic manner, a time is reached when geographic partition is no longer possible. Therefore, the method of presentation now becomes entirely one of chronologic order.

Charaka (early in the first century A. D.), a Buddhist and official physician to King Kaniska, discussed the pulse and, like certain predecessors already mentioned, recognized that the pulse is synchronous with the beat of the heart. He also observed that when death occurred the pulsations ceased. These statements, according to Horine, were found in a Chinese translation of the Buddhist work, Tripitaka.

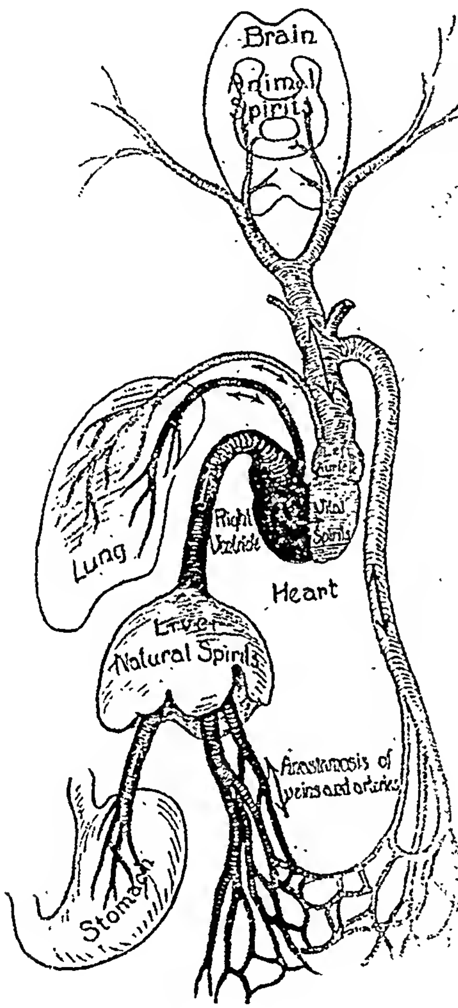
Claudius Galen. (138-201 AD)

Claudius Galen (138–201 A. D.) of Pergamon, Asia Minor, was a noteworthy contributor to the history of cardiology. The details of his life and career have been gleaned from his writings. Galen's anatomic training was acquired under the tutelage of the Hippocratists, Satyrus and Stratonicus. He had held the exalted post of physician to the gladiators but became discontented with the limited opportunities afforded by a small community and sought a broader horizon for his talents in Rome. His interests in medicine were diverse but in this commentary, interest and attention are centered in his beliefs and teachings regarding the heart and circulation. While Galen's concepts pertaining to the heart and circulation were fallacious, no historical documentation would be complete without their inclusion. It is an amazing fact that the almost universal acceptance of his teachings regarding the heart and circulation prevailed for nearly fourteen and a half centuries. This is a remarkable tribute to any man's influence. Even as late as 1649, Jean Riolan or Riolanus (1577–1657), an ardent disciple of Galen, is credited with the statement that if subsequent dissections and observations differed from those of the Master (Galen), any discrepancies were attributable to the fact that nature had changed.

Galen did not possess the fundamental concept of the circulation of the blood and was led into serious error by attempting to fit purely

speculative physiologic conclusions of convenience into inaccurate and incomplete anatomic observations. In other words, the anatomic arrangement of the heart and blood vessels as he knew it must by necessity be able to function.

Galen also held the belief that the blood was formed in the liver from the food ingested. The blood flowed to and from the liver through the veins consisting of the portal vein, the venae cavae (considered as



Galen's concept of the cardiovascular system.

one vessel) and a pouch or diverticulum in the thorax, the right ventricle. The atria were considered to represent only safety outlets from the ventricles. The transportation of this blood back and forth from the liver was accomplished by diastolic aspiration.

At this point it is necessary to diverge from Galen's circulatory mechanism for the moment to recall certain concepts regarding the organism as a whole. Galen, like certain predecessors and contemporaries, accepted the existence of a vital spirit, *anima* or *pneuma*, which was con-

sidered to be the essential principle of life and to be obtained by the act of breathing. It entered the body through the "rough artery" or trachea, reached the lungs and then passed into a veinlike artery (*arteria venalis* [pulmonary vein]) and into the left ventricle.

The blood was formed in the liver from food converted into chyle, absorbed by the mesenteric veins and transported through the portal vein to the liver. In the liver, the chyle was converted into venous blood and endowed with *pneuma.* The blood, thus fortified by both nutritive material and *pneuma,* was then transported through the systemic veins, chiefly the vena cava. Galen held the belief that the vena cava arose from the liver in the same manner that the aorta arose from the left ventricle. The blood, transported by the branches of the vena cava through a continuous process of ebb and flow, carried nutrition and vital spirit to all portions of the body.

In describing the course of the vena cava into the thorax, Galen believed it to terminate in a blind diverticulum which comprised the right atrium and ventricle. As we now resume his reasoning regarding the distribution and destination of the blood that reached this diverticulum in the thorax, two mechanisms of utilization existed. The first assumed that most of the blood lingered for a time in the right ventricle, ridding itself of impurities which had been acquired during its residence in other organs. These impurities were carried off by the *vena arterialis* (pulmonary artery) to the lungs and there exhaled. The blood, thus having cleaned itself, flowed back from the right ventricle by way of the vena cava to the various systemic venous channels. The second concept that Galen offered was to the effect that a small amount of the blood remaining in the right ventricle found its way into the left ventricle by means of invisible pores in the interventricular septum. This concept was one of the most glaring fallacies in Galen's reasoning, for without the concept of either the lesser or the greater circulation, it was the only way in which he could postulate the transportation of blood from the right to the left side of the heart.

In the left ventricle the blood for the first time came in contact with the *pneuma* or spirit of the outside world which had reached the left ventricle by way of the *arteria venalis* (pulmonary vein) from the lungs. This highly purified blood was then distributed by way of the arterial system to all parts of the body.

It is thus apparent that in Galen's physiology of the heart and circulation he was obliged to conjure up substitutes for his ignorance regarding the existence of the pulmonary, systemic and capillary circulations, and in these omissions is found the crux of his errors.

Galen also wrote about the pulse and discussed alterations of the pulse resulting from mild dyscrasias, spoke of sudden death with severe or organic dyscrasias and commented on heart disease in gladiators. He

further wrote about the embarrassing effect of pericardial effusion on the movements of the heart. Galen further described a tumor in the pericardium of a monkey and made comments regarding wounds of the heart, emphasizing that those penetrating a heart cavity were the most serious, especially those of the left heart chambers.

Avicenna (Ibn Sînâ).

Paul of Aegina (625–690 A. D.), the last of the Greek eclectics, wrote an epitome of medicine in seven volumes. In this work he wrote about the pulse and extensively cited the observations and beliefs of Galen. It was translated by Francis Adams (1796–1861) in his "Opus magnum." Paul attributed syncope to disease of the heart.

Kanáda (time not known), an Indian philosopher, also wrote a treatise on the pulse.

Rhazes (Abû Bakr Muhammad ibn Zakariâ [865–925]), a Persian, is classified as the most outstanding physician of his day. In writing on epidemic diseases in his work, "Liber de pestilentia," first published in Valla's "Nicephori logica" collection in Venice (1498), he indicated the importance of the state of the heart in infectious diseases. He called attention to the significance of alterations in the action of the heart, in the pulse, in respiration and in bodily excretions when rendering a prognosis.

Avicenna (Abû Alî al-Hussein ibn Abdallâh ibn Sînâ [980–1037]), another famous Persian physician, was the author of a widely read "Canon of medicine," which consisted of five large volumes. He was the chief physician of the famous hospital at Bagdad and is said to have been a prolific writer. In addition to his medical writings, Avicenna also contributed knowledge to the sciences of geology and chemistry. He wrote extensively about the pulse and is credited with misinterpreting Galen, yet supporting many of his precepts. Avicenna recognized diabetes by the sweet taste of the urine and described the disease. He believed that the heart had three ventricles. He was without a doubt a clever practitioner, as indicated by the extensiveness of his practice and the widespread acclaim which he enjoyed. However, his philosophy, wherein he advocated the superiority of deductive and speculative reasoning over direct observation, exerted an unfavorable influence on the physicians of his day and those of successive generations.

It appears that Avicenna also acted in the capacity of a military surgeon, because Kraus in a report published in 1932 related that he was taken severely ill with colic during a campaign. As the defeat of his troops seemed inevitable and he feared that his illness would prevent a rapid retreat, Avicenna caused himself to be given eight enemas in one day. His condition became worse and a severe dysentery occurred. Avicenna was forced to flee and in his weakened condition, fainted. More enemas were resorted to and a mithridaticum was administered containing opium. His disease became recurrent, he gradually failed and died when he was fifty-seven years of age.

Further comments relating to Arabian medicine will be made in the discussion of the Medieval Era.

SUMMARY

In these historical records covering this somewhat arbitrary period of medical antiquity it is evident that many of the early contributions dealing with the heart and circulation were based on very superficial observations and elaborated by much erroneous speculation. While the early Egyptians did not practice anatomic dissection on cadavers they nevertheless were afforded opportunities to observe certain structures which were revealed when the body cavities were opened in the

preparation of their mummies. Religious prohibitions may have been a deterring influence on the acquisition of anatomic knowledge. The early Egyptians possessed a general idea of the heart and were aware that vessels to various parts of the body were connected with it.

Much attention was focused on the pulse. The ancients detected its relationship to the heart and learned that by counting its frequency and noting its character, certain information could be obtained regarding the status of the heart.

More precise, yet inadequate and erroneous information regarding the anatomy of the heart and blood vessels was forthcoming as anatomic dissections became more frequent. Even in spite of increasing anatomic experience the true status of the cardiovascular system remained obscure, largely because errors of speculation were perpetuated. The most glaring example of this is found in the almost universal acceptance of Galen's errors over a period of nearly fourteen and a half centuries.

Physiologic concepts were largely speculative and frequently were based on incorrect anatomic conclusions. During the Hippocratic era the heart was believed to be immune to disease and it was not until Galen's time that disease of the heart was specifically mentioned.

These primitive observations and deductions, even though incomplete and often fallacious, were nevertheless important, and definitely paved the way for subsequent thought, analysis, reinvestigation and particularly for stimulating interest and the remarkable desire to know and seek the truth in that endless line of scientists who were destined to follow.

It is noteworthy that the medical records of antiquity originated in six essential geographic localities, some of which were contiguous. There were contributions from Egypt, China, Persia, India, Greece and Italy. Little doubt exists that scientific medicine was cradled in Greece and medical nomenclature was largely derived from the Greek language. Greek medicine resulted from centuries of recorded observations, theories and analysis which were fortunately left to medical posterity by the efforts and patience of the great encyclopedists. Early in the sixth century B. C. a fusion of Greek and Southern Italian medicine inevitably took place and progress became accelerated and as Garrison stated, the beginning of European medicine occurred in the succeeding centuries.

REFERENCES

Edwin Smith Surgical Papyrus

Breasted, J. H.: The Edwin Smith Surgical Papyrus; published in facsimile and hieroglyphic transliteration with translation and commentary in two volumes. Chicago, The University of Chicago Press, 1930, vol. 1, 591 pp.

Castiglioni, Arturo: A history of medicine. (Translated by E. B. Krumbhaar.) New York, Alfred A. Knopf, 1941, pp. 55–57.

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, p. 54.
Hamburger, W. W.: The earliest known reference to the heart and circulation; the Edwin Smith surgical papyrus, circa 3,000 B. C. Am. Heart J. 17:259–274 (Mar.) 1939.

Ebers Papyrus

Finlayson, James: Ancient Egyptian medicine [a bibliographical demonstration in the library of the faculty of physicians and surgeons, Glasgow, January 12th, 1893]. Brit. M. J. 1:748–752 (Apr. 8); 1014–1016 (May 13); 1061–1064 (May 20) 1893.
Joachim, H.: Papyros Ebers: Das hermetische Buch über die Arzneimittel der alten Aegypten in hieratischen Schrift. Leipzig, 1875, 2 vols.; also quoted by Finlayson, James.
Joachim, H.: Das alteste Buch über Heilkunde aus dem Aegyptischen zum erstenmal vollständig übersetzt. Berlin, 1890; also quoted by Finlayson, James.

Brugsch Papyrus

Brugsch, Henri: Recueil de Monuments Egyptiens. Leipzig, 1863, pt. 2.
Castiglioni, Arturo: Op. cit., p. 49.
Finlayson, James: Op. cit., pp. 1061–1064.
Garrison, F. H.: Op. cit., p. 54.
Passalacqua: Catalogue raisonné et historique. Paris, 1826, No. 1,558, p. 207; also quoted by Finlayson, James.

Chinese Medicine

Boym, Michael: Quoted by Garrison, F. H., op. cit., p. 75.
Castiglioni, Arturo: Op. cit., chap. 7, pp. 98–112.
Garrison, F. H.: Op. cit., p. 74.

Alcmaeon

Arcieri, J. P.: Alcmeone da Crotone e la scuola Pitagorica. New York, R. Paolella Press, 1937.
Arcieri, J. P.: The circulation of the blood and Andrea Cesalpino of Arezzo. New York, S. F. Vanni, 1945, pp. 17, 19 and 27.
Castiglioni, Arturo: Op. cit., pp. 135–137.
Garrison, F. H.: Op. cit., pp. 89–90.

Dioscorides

Castiglioni, Arturo: Op. cit., pp. 215–217.
Garrison, F H.: Op. cit., pp. 109–110.
White, P. D.: Heart disease. Ed. 3, New York, The Macmillan Company, 1944, p. 955.

Plato

Jowett, B.: The dialogues of Plato. New York, Random House, 1937, 2 vols., 1818 pp.
Osler, William: Aequanimitas with other addresses to medical students, nurses and practitioners of medicine. Ed. 2, Philadelphia, P. Blakiston's Sons & Co., 1920, pp. 47–76.

Hippocrates

Castiglioni, Arturo: Op. cit., pp. 148–178.
Garrison, F. H.: Op. cit., pp. 92–101.

Moorman, L. J.: "We owe a cock to Aesculapius." South. M. J. 25:1197–1202 (Dec.) 1932.
Singer, Charles: A short history of medicine; introducing medical principles to students and non-medical readers. New York, Oxford University Press, 1928, pp. 25–26.

Aegimius

Horine, E. F.: An epitome of ancient pulse lore. Bull. Hist. Med. 10:209–249 (July) 1941.

Aristotle

Arcieri, J. P.: Op. cit. (The circulation of the blood and Andrea Cesalpino of Arezzo), pp. 18 and 29.
Castiglioni, Arturo: Op. cit., pp. 180–181.
Garrison, F. H.: Op. cit., pp. 101–102.
Herrick, J. B.: A short history of cardiology. Springfield, Illinois, Charles C Thomas, 1942, pp. 6 and 14.
Singer, Charles: Op. cit., pp. 27–35.
Vierordt, Hermann: Geschichte der Herzkrankheiten. In Puschmann, Theodor: Handbuch der Geschichte der Medizin. Jena, Gustav Fischer, 1903, vol. 2, pp. 631–647.

Praxagoras

Arcieri, J. P.: Op. cit. (The circulation of the blood and Andrea Cesalpino of Arezzo), pp. 19, 20 and 69.
Castiglioni, Arturo: Op. cit., p. 180.
Garrison, F. H.: Op. cit., pp. 101 and 103.
Horine, E. F.: Op. cit., p. 210.

Herophilus

Arcieri, J. P.: Op. cit. (The circulation of the blood and Andrea Cesalpino of Arezzo), pp. 18, 19 and 69.
Breasted, J. H.: Op. cit., p. 13.
Castiglioni, Arturo: Op. cit., p. 185.
Garrison, F. H.: Op. cit., pp. 100, 103 and 104.
Herrick, J. B.: Op. cit., p. 8.
Horine, E. F.: Op. cit., p. 211.
Singer, Charles: Op. cit., p. 36.
Vierordt, Hermann: Op. cit., p. 631.

Erasistratus

Castiglioni, Arturo: Op. cit., pp. 185–187.
Garrison, F. H.: Op. cit., pp. 103 and 246.
Herrick, J. B.: Op. cit., pp. 8–9.
Horine, E. F.: Op. cit., p. 211.
Vierordt, Hermann: Op. cit., pp. 631–632.

Celsus

Castiglioni, Arturo: Op. cit., pp. 204–213.
Garrison, F. H.: Op. cit., pp. 107–109.
Herrick, J. B.: Op. cit., pp. 7, 8 and 147.
Horine, E. F.: Op. cit., pp. 215–216.

Seneca

Gibson, G. A.: Diseases of the heart and aorta. New York, The Macmillan Company, 1898, 932 pp.

Gibson, G. A.: Original communications. The nervous affections of the heart. Edinburgh M. J. n.s. 12:9–24; 141–155; 405–414, 1902.
Seneca, L. A.: Opera, Basileae, Epist, 55, 1529; also quoted by Allbutt, Clifford: Diseases of the arteries including angina pectoris. London, Macmillan and Company, Limited, 1915, vol. 2, p. 319.
Willius, F. A.: Cardiac clinics. CXII. The historic development of knowledge relating to the coronary circulation and its diseases: introduction and the preharveian era. Proc. Staff Meet., Mayo Clin. 20:103–106 (Apr. 4) 1945.

Rufus

Arcieri, J. P.: Op. cit. (The circulation of the blood and Andrea Cesalpino of Arezzo), p. 69.
Castiglioni, Arturo: Op. cit., p. 215.
Garrison, F. H.: Op. cit., pp. 111 and 123.
Gibson, G. A.: Op. cit. (Diseases of the heart and aorta), pp. 174–175.
Horine, E. F.: Op. cit., p. 216.

Archigenes

Castiglioni, Arturo: Op. cit., pp. 247 and 379.
Garrison, F. H.: Op. cit., pp. 107, 109 and 110.
Horine, E. F.: Op. cit., p. 217.

Charaka

Castiglioni, Arturo: Op. cit., p. 87.
Horine, E. F.: Op. cit., p. 230.

Galen

Arcieri, J. P.: Op. cit. (The circulation of the blood and Andrea Cesalpino of Arezzo), pp. 20–24, 32, 33, 35, 37, 40, 42, 47, 49, 54, 64, 66, 68, 74, 80, 100, 101, 116 and 133.
Castiglioni, Arturo: Op. cit., pp. 217–226.
Garrison, F. H.: Op. cit., p. 248.
Glomset, D. J.: Romances or cardiology. J. Iowa M. Soc. 35:52–58 (Feb.); 96–102; 114 (Mar.) 1945.
Herrick, J. B.: Op. cit., pp. 4, 6, 8–11, 13, 14, 17, 21, 38, 166 and 208.
Horine, E. F.: Op. cit., pp. 210, 211, 220, 221 and 223.
Singer, Charles: Some Galenic and animal sources of Vesalius. J. Hist. Med. & Allied Sc. 1:6–24 (Jan.) 1946.
Willius, F. A. Cardiac clinics. CXIII. The historic development of knowledge relating to the coronary circulation and its diseases. II. Harvey and the seventeenth century. Proc. Staff Meet., Mayo Clin. 20:155–156 (May 16) 1945.

Paul of Aegina

Castiglioni, Arturo: Op. cit., pp. 253–255.
Garrison, F. H.: Op. cit., p. 124.
Herrick, J. B.: Op. cit., p. 10.
Vierordt, Hermann: Op. cit., p. 632.

Kanáda

Horine, E. F.: Op. cit., p. 230.

Rhazes

Castiglioni, Arturo: Op. cit., pp. 267–270.
Garrison, F. H.: Op. cit., p. 129.

Herrick, J. B.: Op. cit., p. 10.
Singer, Charles: Op. cit. (A short history of medicine), pp. 67 and 70.

Avicenna

Castiglioni, Arturo: Op. cit., pp. 270–273.
Garrison, F. H.: Op. cit., pp. 129–131.
Herrick, J. B.: Op. cit., p. 11.
Kraus, Paul: Quoted by R., W.: The death of Avicenna (980–1037). Ciba Symposia. 6:1883 (Oct.) 1944.
Singer, Charles: Op. cit. (A short history of medicine); pp. 67, 70, 72, 74 and 82.

THE MEDIEVAL ERA

*The medical errors of one century constitute the popular faith of the next.**

THE MEDIEVAL ERA of civilization is alternatively known as the Middle Ages, which is the period between antiquity and the Renaissance (approximately from 1096 to 1453 A. D.). Some historians appropriately object to the designation, Medieval, as that term is commonly applied to indicate an era of human unenlightment or to the Dark Ages. This belief, to a great degree, was sponsored by the historians of the Renaissance, who in their attitude of virtuous superiority, saw no good in the preceding era. While this period in history had its dark side, the seeds of enlightment had nevertheless already been sown, and while only sprouting, were destined to flourish and grow with the succeeding generations of man. Here, as well as in the progressive development of the text, it is important to bear in mind that in the transition from one era to another, or from one century to the next, the events occur in a precise chronologic order but precise in that sense only. Changes in human development, concepts, beliefs, ideals, and so forth, are extremely gradual and this subtle evolution not only is apparent in the early periods of history but is likewise operative today.

The Medieval Era was one of profound upheaval: social, political, economic and religious, affecting virtually all human activities, which influenced practically all existing civilization. Europe was devastated by wars, epidemics flourished, famines occurred and the earlier invasion of the barbarians had literally completed the devastation of a remarkable culture and its physical assets. Christianity had been born and a new force in the form of ecclesiastic influences was becoming more stringent and repressive on all human activities.

In the early centuries after the triumph of Christianity the practice of medicine had been largely within the province of the ecclesiastics and it was not until the early part of the ninth century that medicine, in a limited manner, passed into the hands of the laity. The assertion of even this small degree of medical independence coincided with the founding of the school of Salerno. Hitherto, as illustrated by the long-existent barrier between Greek and Italian medicine, the voluntary interchange of ideas and knowledge between nations was practically

* Alonzo Clark (1807–1887), cited by Garrison.

nonexistent. The basic concept of the Salernitan school was in direct opposition to this existing self-sufficient and cloistered philosophy. Its intention was to seek deliberately the beliefs and teachings of many physicians and teachers so that the best of existent knowledge could be put to constructive use. The result was that Greeks, Italians, Jews, Arabs, Orientals and the monks of western Europe united to build this famous Italian institution of learning. It was at this point that the laity secured a firm grasp on medicine which gradually increased, while the ecclesiastics progressively lost control, but continued to exert various prohibitions for many centuries to follow. Finally, in the beginning of the thirteenth century, medicine was almost entirely under the influence and leadership of the laity. Salerno reached its peak of eminence in the twelfth and thirteenth centuries and was honored and revered throughout the civilized world.

The Holy Roman Empire, including Italy and Germany, under the rule of Frederick II, the grandson of Frederick I (Barbarossa), gave constructive impetus to medicine. Frederick II, who ruled from 1215 to 1250, initiated the idea of licensing physicians to practice their profession and issued certain edicts to improve medical teaching. He vested the sole right of granting licenses in the Salernitan school and further, commanded that the study of anatomy by means of dissection on cadavers should comprise an important part of teaching.

While much of the era was characterized by retrogression some sporadic growth of science and culture had occurred. In view of the many upheavals and deterring influences it is not remarkable that little progress and development occurred in medicine and other sciences. Very few contributions dealing with the heart and circulation emerged from this era.

In certain parts of the civilized world the impact of these chaotic conditions was not as great and this was particularly true in the Arab provinces. Thus, a brief commentary regarding early Arabian medicine may help to orientate the reader regarding subsequent remarks. Already in the preceding era we have discussed the Persians, Rhazes, and Avicenna, and while chronologically they lived in the era of Antiquity only a few centuries separated them from contributors in this period.

It was through the might of Mohammed (567–632) and his emirs that the wild tribesmen of the African and Asian deserts were converted into units which gradually assumed their role in the world's civilization. The Mohammedans received their first medical knowledge from a persecuted group of Christians who had sought refuge in the desert. These Christians had first gone to Edessa in Mesopotamia where they established a medical school but were later forced to leave owing to presumed heresies. They next fled to Persia where they originated a famous school at Gondisapor.

During the eighth and ninth centuries in the reign of the caliphs Al-Mansur, Harun al-Rashid and Al-Meiamun, the accumulation of medical knowledge from other nations was encouraged. Greek medical literature was particularly in demand and translations were made from the works of Hippocrates, Galen, Dioscorides and others. Arabian medicine was the outgrowth of the medicine of many peoples. Many Spanish Arabs migrated to the eastern Arabian countries and some of them materially aided the scientific and cultural development of the Near Eastern races.

The greatest of all Spanish Mohammedan physicians, of Jewish ancestry, frequently referred to as the "Famous Wise Man," was Avenzoar (Ibn Zuhr) (1113–1162). He was born in Cordoba (Cordova), Spain, spent most of his life in Arabia and ultimately returned to his native country. His death occurred in Seville. Avenzoar was violently opposed to the deductive speculations of Avicenna, which were still prevalent, and publicly disagreed with Galen, a courageous act in that day and age. Avenzoar described serofibrinous pericarditis. In his work, "Altheisir," Lib. I, Tract XII, several references to the heart were found. He discussed diseases of the heart, distinguished between primary disease and sympathetic disorders and also commented on the relative importance of the right and the left ventricles, concluding that the latter was the more important.

Avenzoar referred to palpitation of the heart and discussed *malum cardiacum.* This latter term is likely a variant of *morbus cardiacus,* which haunted early medical literature and the exact meaning of which is unknown. Herrick suggested that the term probably referred to several conditions concerned with both the heart and other viscera. Avenzoar also described pericardial effusion, spoke of erysipelas of the heart and abscess of the heart. Bloodletting was important in his therapeutics.

Bartolommeo Montagnana was a professor at Padua from 1422 to 1441. He was a highly esteemed surgeon and was said to have dissected at least fourteen human bodies. Montagnana described strangulated hernia, repaired a lacrimal fistula and extracted carious teeth. His observations pertaining to the heart are of interest. Among these observations was one ascribing cough to disease of the heart and it is not unlikely that he had observed this symptom in the passive congestion of the lungs accompanying heart failure. In describing what appeared to be heart failure he wrote of *motus tremulans et bipulsans cordis.* It is possible that Montagnana had observed the pulse irregularity of auricular fibrillation.

Without a doubt, the most outstanding contribution up to this time was that of Ibn an-Nafis,* dean of the Mansoury Hospital in Cairo (see special biography). Ibn an-Nafis lived in the thirteenth century (circa

* Owing to composition problems, i is used in Arabic names in place of ī.

1210–1288). Owing to the importance of his work and its regrettable submersion in medical history until very recent years, special biographic emphasis will be accorded him. He was the first to describe accurately the pulmonary circulation, a discovery usually credited to Michael Servetus (1553). It is most plausible, as indicated by Temkin, that Servetus' conclusions regarding the pulmonary circulation were original, for it would have been a rare coincidence for him to have known of this earlier work either through word of mouth or written manuscript, nor does this prior contribution detract in any measure from the lucid thinking and deductions of Servetus. Ibn an-Nafis denied the existence of Galen's "invisible pores" in the interventricular septum while Servetus made no reference to them.

Ibn an-Nafis' description of the pulmonary circulation appeared in his "Commentary on the anatomy in the Canon of Ibn Sînâ" Shash Tashrih al-Qānūn li-'bn Sinā). The circulation was clearly described five times and Ibn an-Nafis discussed the general physiologic principles of respiration. He classified man as an air-breathing creature in whose lungs the aeration of the blood occurred. The alveoli of the lungs were mentioned (first demonstrated by Malpighi in 1660). Ibn an-Nafis also stated that the heart was nourished by its own vessels, thus presenting a very early record of the coronary circulation.

The following quotations in translation from Meyerhof's commentary are significant: "Therefore, *the blood,* after having been refined, *must rise in the arterious vein to the lung in order to expand its volume and to be mixed with air* so that its fumes and part may be clarified *and may reach the venous artery in which it is transmitted to the left cavity of the heart.*" And discussing the two ventricles he stated: "*But there is no passage between these two cavities;* for the substance of the heart is solid in this region and has neither a visible passage, as thought by some persons, nor an invisible one which could have permitted the transmission of blood, as was alleged by Galen."

Ibn an-Nafis contended that the right ventricle was not dynamic and that it was inconsequential whether or not the heart was designated as a muscle. He stated that the heart had two ventricles and this is an important consideration because others had denied this fact. It should be recalled that Aristotle claimed that the number of ventricles varied with the size of the animal while Avicenna asserted that three ventricles were present.

While contributions dealing with the heart and circulation were few in this unsettled and unhappy era, the significance and importance of Ibn an-Nafis' discovery and description of the pulmonary circulation, by itself, glorify this otherwise drab period of medical history. This era still antedated the science and the art of printing and all records were inscribed by hand using parchment and similar writing material.

Thus, a limited literature existed, consisting of laborious inscriptions, available only to a select few.

REFERENCES

Arabian medicine

Haddad, S. I.: Arabian contributions to medicine. Ann. M. Hist. s. 3, 3:60–72 (Jan.) 1941.

Avenzoar

Castiglioni, Arturo: A history of medicine. (Translated by E. B. Krumbhaar.) New York, Alfred A. Knopf, 1941, pp. 276–277.

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, p. 132.

Herrick, J. B.: A short history of cardiology. Springfield, Illinois, Charles C Thomas, 1942, p. 11.

Vierordt, Hermann: Geschichte der Herzkrankheiten. In Puschmann, Theodor: Handbuch der Geschichte der Medizin. Jena, Gustav Fischer, 1903, vol. 2, pp. 632–633.

Montagnana

Castiglioni, Arturo: Op. cit., p. 366.

Herrick, J. B.: Op. cit., p. 11.

Vierordt, Hermann: Op. cit., p. 633.

Ibn an-Nafis

Haddad, S. I. and Khairallah, A. A.: A forgotten chapter in the history of the circulation of the blood. Ann. Surg. 104:1–8 (July) 1936.

Meyerhof, Max: Ibn an-Nafis (XIIIth cent.) and his theory of the lesser circulation. Isis. 23:100–120, 1935.

Temkin, Owsei: Notes and comments: Was Servetus influenced by Ibn an-Nafis? Bull. Hist. Med. 8:731–734 (May) 1940.

3

THE RENAISSANCE

*But like a man walking alone in the darkness I resolved to proceed so slowly and carefully that, even if I did not get very far, I was certain not to fall.**

CIVILIZATION was slow in its recovery from the upheavals, destruction and unrest of the preceding centuries. Historians apply the term "Renaissance" to that period of the world's history which bridged the gap between the so-called Middle Ages and modern civilization. No concise dates can be assigned to this period although the century and a half from 1453 to 1600 approximately embraces the era under consideration. The processes of evolution are slow and while some progress occurred in the Medieval Era, its full effect was not apparent until later.

The indomitable courage, determination and resourcefulness of man refused to be repressed permanently by the forces of prejudice, of traditional unenlightenment and of superstition. It is, therefore, not remarkable that the prevailing inertia of spirit, thought and endeavor should undergo a change. Even in the early portion of the Medieval Era there appeared considerable evidence of intellectual awakening. This was particularly manifest in the creation of the school of Salerno, which coincided with the emancipation of medicine from the absolute control of the clergy and the passage of more control to the laity. While many restrictions and prohibitions remained, a greater freedom of thought, purpose and action became possible.

The Renaissance was the period of the rebirth of science, literature and the arts. A trend toward again embracing the classics and the culture of a glorious and extinct civilization became evident. As after other biologic hibernations, the process of reactivation was gradual but certain. Medicine, like the other sciences, forged ahead, and this new era contributed many important discoveries. In their development the field of the heart and circulation shared in a significant measure.

Anatomic studies by means of dissection became more frequent and accurate so that gradually the general structure of the human body became unfolded. Anatomic illustration was born, chiefly through the craftsmanship of Leonardo da Vinci and Stephen Calcar, and thus the graphic method of teaching came into being. Physiologic progress was slow and was still largely confined to speculation. The lot of the scientist was still difficult and discouraging because not all the restrictions of the

* René Descartes (1596–1650) cited by Garrison, p. 14.

previous era had been eliminated. Religious prohibitions still exerted their deterring influences and scientific utterance frequently provoked the charge of heresy.

The dissemination of knowledge was slow and the written word was still recorded in manuscripts which were tedious and time-consuming in their preparation and so costly as to be beyond the ownership of many. Some discoveries and observations were recorded in letters available only to a privileged few. Printing* came into being during this era and was a powerful influence in the dissemination of knowledge and the interchange of scientific thought. The pioneer methods of printing were slow, laborious and costly. Gutenberg, who discovered the method of casting movable type so that it could be set up in rows to form lines and pages, utilized it in a hand press. Each printed page required tedious resetting and the making of the type was all done by hand. Paper was still scarce and costly with the result that the production of books occupied much time and when finally completed the books were very expensive. The type, for reasons of economy, was often very small and individual letters lacked conformity. Gutenberg's efforts resulted in his falling deeply in debt and it is said that his creditors seized all his equipment, which they used to their own advantage, while the discoverer died in poverty. Within half a century after Gutenberg's discovery, however, the science and the art of printing had spread throughout Europe.

Nicholas Krebs of Cues, the Cardinal Cusanus (1401–1464), a Roman Catholic churchman of broad vision and an accomplished mathematician, published his "Dialogue of statics" in 1450. In this work he advocated carrying out estimations of the weight of the blood and urine. This concept constituted one of the earliest attempts at sound physiologic reasoning and measurement. His suggestions, however, were not put into use for many generations. Krebs also used a water clock to count the pulse (a method already applied by the early Egyptians and later by Herophilus) and respiration in both health and disease.

Toward the close of the fifteenth century anatomic dissection on cadavers was officially authorized by a bull of Pope Sixtus IV who held his post from 1471 to 1484. He had studied both at Padua and at Bologna. This edict of scientific liberalism greatly aided and stimulated the development of anatomic research. It was not long thereafter that one of the pioneer works on anatomy appeared.

Alessandro Benedetti (1460–1525), who succeeded Gabriele Zerbi as professor of anatomy at Padua, published an "Anatomia" in 1497. This work consisted of five books. In 1493 he described a case of malposition of the heart. This was in all probability the first report of its kind.

* According to Garrison, the priority of the invention of the printing press is divided between Laurens Janszoon Coster, of Haarlem (1440) and Johan Gutenberg, of Mainz (1450).

Benedetti is believed to have been the founder of an anatomic theater at Padua, where he lectured and conducted public demonstrations.

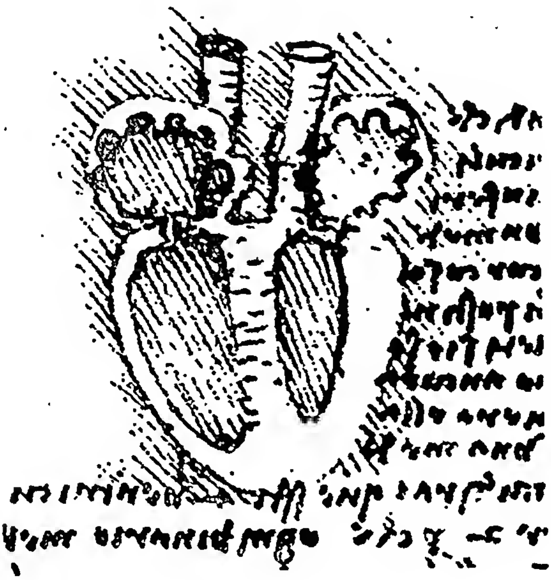
A contemporary of Benedetti, and presumably his teacher, Antonio Benivieni (circa 1440–1502) also contributed to this period of medical history. He was a noted surgeon and practitioner of Florence and is described as founder of pathology before Morgagni. However, his contributions in this field cannot be compared with those of the great Morgagni. Benivieni's work, "De abditis nonnulis ac mirandis morborum et sanationum causis," was posthumously published by his brother in 1507 from the Giunta Press. He observed in the cavities of the heart postmortem thrombi, which he erroneously conceived and described as cardiac polyps. This declaration was the beginning of a pathologic controversy which raged for many years. Benivieni also observed the thick, stringy deposits of fibrin in fibrinous pericarditis and described the changes as a structure loaded with hair. In "De abditis causis" he reported on twenty postmortem examinations, in reality the first attempt to discover the cause of disease by dissection.

Leonardo da Vinci (self-portrait).

Probably the most outstanding and gifted personality of the Renaissance and for years thereafter, was the fabulous Italian, Leonardo da Vinci (1452–1519). In medical history he is known as the greatest artist and physiologic anatomist of his time and the father of medical illustration. However, before expounding his medical achievements it would be amiss not to consider his other multitudinous talents and interests. An artist of rare instincts and emotions, he obtained his first instruction as an apprentice to the famed painter and sculptor, Verrocchio of Florence. Leonardo ultimately exceeded the brilliance of his master.

Two of Leonardo's paintings remain today among the world's greatest masterpieces, "The Last Supper," painted on the wall of a Milanese convent refectory, and "Mona Lisa" (La Gioconda). Also a sculptor, he undertook to create a great equestrian statue for the ducal house of Sforza but this was never completed because the large model was destroyed by the invading French.

In addition to his artistic accomplishments, Leonardo was a genius in geology, geography, astronomy and engineering. He planned great engineering projects to control the course of both the Po and the Arno rivers and conceived the general idea of an airplane and of an underwater craft. He destroyed the latter plans when he realized the possibilities of its use as a weapon of destruction. Leonardo devised a portable bridge for military operations, a suction pump for emptying moats in the siege of castles and had plans for a self-propelled armored vehicle. He cast a cannon composed of thirty-three barrels, eleven of which could be discharged simultaneously, and designed rapid fire guns, conical shells, grapeshot and shrapnel.



Drawing of a heart by Leonardo da Vinci showing his representation of the "invisible pores" in the interventricular septum.

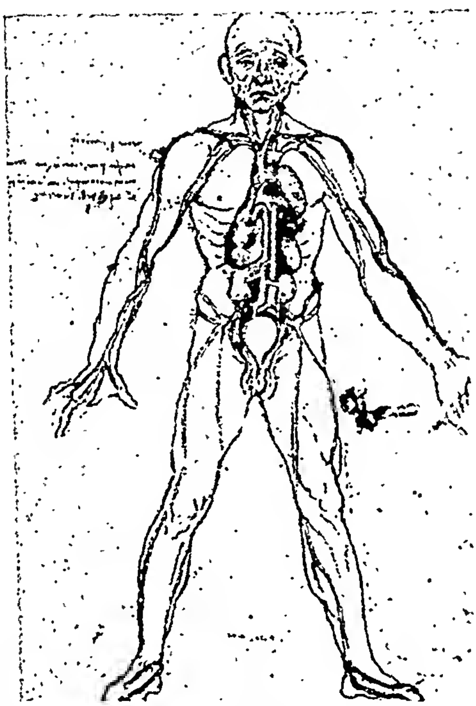
This fabulous man also made fuses and hand grenades and planned gas bombs and protective gas masks, calculated the trajectory of missiles and devised a mechanism for raising and lowering guns to compensate for errors in range. He mounted cannon on wheels and substituted breech loading of guns for the cumbersome method of muzzle loading.

Leonardo also conceived the idea of a prefabricated portable house, designed an earth drill and mounted a magnetic needle on a horizontal axis, thereby constructing the first compass. He invented a wind gauge, is said to have announced the theory of light, sound and centrifugal force, suggested the atomic theory of matter and conceived the idea of explosive bombs.

Of Leonardo's superb anatomic drawings more than 750 were executed in chalk. They remained buried for more than two centuries and

it is likely that many were not preserved and still more are as yet undiscovered. The drawings showed, in addition to the general characteristics of the heart, the large coronary vessels and their main tributaries. In at least one of his drawings of the heart, Leonardo attempted to schematize the "invisible pores" of Galen in the cardiac septum. He conceived the heart as a pump and like certain predecessors he maintained that the heart beat and the pulse were synchronous. He also discovered and described the moderator band of the heart.

Leonardo made hundreds of sketches before making his final drawing or painting. It is said that he followed and sketched people under all conditions and actions of life in order to obtain realistic posture, facial



The cardiovascular system, by Leonardo da Vinci.

expression, muscular configuration, and so forth. He sketched people in prayer, old folks during death and criminals at the time of their execution. Many of his works were never completed because apparently his active and fertile mind always goaded him to new endeavors. He considered the muscles of the body as levers and the eye as a lens. Leonardo also ascribed the death of many aged people to what is now known as arteriosclerosis.

Leonardo was left-handed and devised a peculiar script which he recorded from right to left but later he became ambidextrous. History does not authenticate how many of Leonardo's innovations were actually created, how many remained recorded on paper and how many remained engraved in his remarkable mind. This great man's construc-

tive imagination has never been surpassed and there is little doubt that he was a modern, living about five hundred years before his time.

Further anatomic contributions concerning the structure of the heart were forthcoming, particularly from the illustrious line of Italian anatomists.

Jacopo Berengario da Carpi (1470–1550) was professor of anatomy at Bologna from 1502 to 1522. Later he became a very successful practitioner in Ferrara. He was one of the first anatomists to illustrate his works with excellent engravings. Prior to the artistry of Leonardo da Vinci, illustrations were chiefly of a surrealistic schematic character resembling the scrawling delineations of a small child. Da Carpi described the cardiac valves in his "Isagogae" which was published in 1522. He conducted one of the earliest experiments concerned with the injection of arteries, in which he filled them with tepid water in order to follow their course. In 1521, da Carpi wrote a "Commentary on the Anatomy of Mondino" and in this work he mentioned dilatation of the heart.

The heart after da Carpi, from "Isagogae."

He was among the first to employ mercurial ointment in the treatment of syphilis, he described the sphenoid sinuses, the tympanic membrane, the pineal gland, the appendix, the arytenoid cartilages, the lateral ventricles of the brain and the choroid plexus.

In 1523, Thomas Linacre (1460–1524), a graduate of both Padua and Oxford, contributed an exhaustive treatise on the pulse, "De pulsuum usu," printed by Pynson of London. This work was largely a Latin translation of Galen's works. Linacre was a scholar of note, accurately translated many early works and was particularly known for his rhetoric precision. It has been suggested that he was the subject of Robert Browning's "Grammarian's Funeral." Linacre lectured on medicine both at Oxford and Cambridge and through his influence and charming personality is credited with restoring learning and culture to England. He was personal physician to Henry VII and Henry VIII.

A discussion of this period of history would be incomplete without mention of one of the most colorful personalities of the Renaissance. While not adding directly to the knowledge of the heart and circu-

lation, Paracelsus made certain important contributions to his era, particularly in breaking down numerous outmoded yet still prevailing customs. Born in Einsiedeln, Switzerland (1493–1541), he was named Philippus Theophrastus Bombastus von Hohenheim. He adopted the name "Paracelsus," presumably because he thought himself intellectually superior to the famous Celsus of the early Christian era. Furthermore, he seemed to like the prefix "para-," because it was freely used in the titles of his writing. Plainly an extrovert, Paracelsus had little or no regard for the beliefs and teachings of others, despised tradition and was harsh in his criticism of everything conventional. When still a young man, he displayed his contempt for the orthodox acceptance of prevailing medical knowledge by publically burning the works of Avicenna, Galen and others. Paracelsus was a curious mixture of fact and fancy: the practical acceptance of natural phenomena on the one hand and a strong tendency to mysticism on the other. He was an advocate of the Doctrine of Signatures; yet was possessed of a natural inquisitiveness which prompted him to learn the truth whenever possible.

Thomas Linacre.

Paracelsus shattered all existing customs by both writing and lecturing in his native tongue rather than in the formal and scientifically accepted Latin. He was the author of more than 300 separate works. He was one of the first to use mercury in the treatment of syphilis and described and discussed "tartaric" states which included diseases producing pathologic secretions, concretions, calcifications and other abnormal deposits. Further, Paracelsus recognized the predisposition of patients to certain diseases, such as gout, rheumatism and arthritis, and placed such diseases in a specific category. Many of these observations were recorded in his "Paragranum," which first appeared in 1530.

In his work, "De generatione stultorum," Paracelsus related cretinism with endemic goiter. He was violently opposed to galenic therapy and introduced various chemicals, such as copper sulfate, potassium sulfate, mercury, lead, sulfur, iron and arsenic, in the treatment of disease. He described the pulmonary changes in miners in his work "Von der

Bergsucht," published posthumously at Dilingen in 1567. Paracelsus recorded observations on epilepsy, related paralysis and speech defects to injuries to the head and compared apoplexy to a stroke of lightning.

A wanderer, a scientist, a mystic, an antagonist of prevailing doctrines and beliefs, a man possessed of a keen intellect and unusual inquisitiveness, Paracelsus literally blasted a wide path through the wilderness of prevailing orthodoxies. His shattering of conventional barriers unmistakably made the progress of his successors easier and smoother.

Nicolo Massa (?–1569), of Padua, was one of the outstanding syphilographers of his day and attracted patients from all over Europe. He is believed to have been the first to describe gummata and believed that the disease could be transmitted by soiled linen. Massa's work on syphilis, "De morbo gallico," was published in Venice in 1532. He recorded an interesting observation on the heart in his book, "Liber introductorius anatomiae," Chapter XXII (circa 1534), where he described a swelling involving both sides of the heart which resulted in great enlargement of the organ. This probably was an early account of cardiac hypertrophy.

Paracelsus.

The high light of Renaissance anatomy rested on the works of Andreas Vesalius (1514–1564), the most brilliant of the long line of Paduan anatomists. Vesalius was of Flemish birth and German ancestry. According to Garrison, he was the most commanding figure in European medicine after Galen and before Harvey. Vesalius' most famous work, "De fabrica humani corporis," published in 1543, was superbly illustrated by the celebrated artist, Stephen Calcar. However, as Singer has pointed out, Vesalius' anatomy consisted of an admixture of animal and human dissections. This is clearly demonstrated by the illustrations in his work with special reference to the bones and muscles. As Singer further stated, "The anatomical vision of Vesalius was thus perforce a patchwork construction. Its basis was necessarily the dissection of animals and perhaps of still-born children." While Vesalius unquestionably dissected human bodies his experience with animal anatomy, especially with the structure of the Barbary ape (Macaca inua), was far more extensive. Furthermore, he

knew only the erroneous physiologic concepts of Galen with reference to the heart and circulation. As previously stated in this work, the blind acceptance of Galen's beliefs retarded both anatomic and physiologic progress for nearly fourteen and a half centuries, and many able anatomists were led astray by faith and thereby perpetuated the errors of a previous era.

Vesalius described the course of the veins and the general structure of the heart, and demonstrated the coronary vessels. He disagreed with Galen in his admission that he had not been able to demonstrate pores in the septum of the heart. Vesalius made the demonstration that the life of an animal could be sustained by artificial respiration after the thorax had been opened. He also showed that on occasions, the non-beating heart could be resuscitated by the use of bellows. Vesalius was the first to recognize and describe aneurysm of the thoracic and abdominal aorta (1555). His influence in medicine prevailed for many years, as testified by the citations of his work in publications as late as the beginning of the nineteenth century.

Andreas Vesalius.

Giovanni Battista Canano (1515–1579), of Ferrara, was a contemporary of the famous Vesalius. He was a great anatomist, and according to Castiglioni, he, rather than Vesalius, was the first actually to demonstrate the valves of the veins, a discovery frequently credited to Vesalius. Canano was in the process of writing an extensive treatise on anatomy when Vesalius' "De fabrica humani corporis" appeared. Apparently realizing the futility of attempting to equal or excel this work, Canano compiled and published only one section of his treatise, "Musculorum humani corporis picturata dissectio," published at Ferrara near the close of the first half of the sixteenth century.

Guido Guidi (Vidius) (?–1569), a Florentine by birth, was royal physician and professor at the Collège de France. In 1547 he was recalled to Italy and accepted the professorship of philosophy and medicine at Pisa. Guidi contributed a work on surgery "Chirurgia e Graeco in Latinum conversa," which was published in 1544. He disproved Galen's erroneous assumption regarding the existence of invisible pores

in the cardiac septum, an implication that he held an insight at least of the existence of the lesser circulation. Two anatomic structures bear his name, the vidian nerve and the vidian canal.

Another distinguished anatomist of this era was the Frenchman, Carolus Stephanus (Charles Estienne) (circa 1500–1564). He was a pupil of the celebrated anatomist, Sylvius, and a member of a family of famous printers. In his extensive work, "De dissectione partium corporis humani," published in Paris, in 1545, he also described the valves of the veins and referred to them as *apophyses membranarum.*

One of the dramatic yet pathetic figures of the Renaissance was Michael Servetus (1509–1553), of Villanueva de Sigena (see special biography). He was the hapless martyr who met death on the pyre, and described the pulmonary circulation in his famous religious work, "Restitutio Christianismi," 1553.* Servetus' exposition of the pulmonary circulation appeared about three centuries after Ibn an-Nafis' description. As previously stated, there is no reason to believe that Servetus knew of this earlier work and while history records a priority for Ibn an-Nafis, neither of these contributions exerted a pronounced influence on Galen's fallacious teachings. The contribution of Servetus is probably better known than that of Ibn an-Nafis because he lived in a somewhat later age and in a less remote portion of the world but largely because his martyr's death attracted much attention at the time and since in historic documentation.

Jean Fernel.

The outstanding physician of the French Renaissance was Jean Fernel (1506–1588). He was a graduate of Paris and later became professor of medicine at Paris. Fernel was an anti-Galenist and his influence and sound reasoning did much to destroy the prevailing acceptance of Galen's views in France. He was thoroughly schooled in mathematics

* Mackall brings forth evidence to the effect that "Restitutio Christianismi" was written and in circulation by 1546, at least thirteen years prior to Colombo's publication. Leonard L. Mackall, "A manuscript of the 'Christianismi Restitutio' of Servetus, placing the discovery of the pulmonary circulation anterior to 1546," Proc. Roy. Soc. Med. (Section of the History of Medicine). 17(pts. 1 and 2): 35–38 (Oct. 17) 1923.

and philosophy, and for several years wasted much time by dabbling in astronomy. However, he eventually spent more time with medicine and less with planetary matters and became an unusually successful practitioner of medicine.

Among Fernel's works was his famous "Universa medicina," which was published in 1554. It was divided into three parts, physiology, pathology and therapeutics. Together with many other observations was his belief that aneurysms were produced by syphilis. He was the first to associate arterial dilatation with aneurysm and differentiated true from false aneurysms. Fernel did not accept the view that the artery was ruptured. Postmortem observations were included in this work.

In 1567, Fernel described "iliac passion" supported by postmortem findings which constituted one of the earliest recorded instances of appendicitis. He was opposed to indiscriminate bloodletting, a practice extensively employed in his time.

Ambroïse Paré.

A contemporary of Fernel was Ambroïse Paré (1510–1590). He was a celebrated French surgeon who contributed generously to his field. Paré made Vesalius' "De fabrica humani corporis" practical and popular for the surgeon by writing a commentary in his native language. In 1537 he became an army surgeon and attained great fame for his ability and courage. Like Fernel, Paré associated syphilis with aneurysm. He deplored the incision of aneurysms or the application of caustics to superficial masses, which was frequently done by the barber-surgeons. Paré uttered the warning that when incision was considered, the skin should be carefully incised, the tissues cautiously separated until the artery was exposed and then with a blunt, crooked needle and thread the sac could be tied off. In time, nature covered the area with "new flesh" and a simple cure could be effected. He wrote extensively on surgical subjects and devised instruments. Among these contributions was the treatment of gunshot wounds (1545), description of podalic version (1550) and an extensive treatise on surgery (1564). Paré was probably the first to ascribe the transmission of infectious diseases to flies. He was surgeon to Henry II, Francis II and Charles IX.

Jacques Dubois (Sylvius) (1478–1555) was Vesalius' teacher at Paris. A bigoted individual, he remained a fanatical adherent of Galen's views in spite of constantly growing opposition and enlightenment. Sylvius violently disagreed with Vesalius and insisted on perpetuating Galen's errors. He, nevertheless, contributed to the anatomy of the cardiovascular system in his "Isagoge," published in Venice in 1556 shortly after his death. In this work, Sylvius named the jugular, subclavian, renal, popliteal and other vessels. He also mentioned the valves of the veins and was the first to mention the sylvian aqueduct, which bears his name.

In respect to the works of Matteo Realdo Colombo (Columbus) (1516?–1559), of Cremona, another controversy regarding priority and plagiarism occurred among historians. Colombo was Vesalius' successor at Padua. In his work, "De re anatomica," published in 1559, he described the pulmonary circulation but evidently did not correctly conceive the details because he held the view of the ancients that the veins carried the nutritive blood throughout the body and adhered to Galen's belief that the liver was the central organ of the cardiovascular system. Colombo's work appeared six years after the death of Servetus and about three centuries after Ibn an-Nafis' description of the pulmonary circulation. In view of the fact that some evidence exists that Colombo plagiarized Vesalius' work in that he imitated the title page of "De fabrica" and utilized other characteristics of this book, the question has naturally been raised among medical historians whether the same was not true with respect to Servetus' work.


Jacques Dubois (Sylvius).

Colombo demonstrated by vivisection that the pulmonary veins contain blood but held the belief that the blood became cooled during the process of respiration, a contention of the ancients. He also contended that Galen's belief in the existence of "invisible pores" in the septum of the heart was a myth.

Another eminent Italian anatomist of this period was Gabriele Falloppio (Fallopius) (1523-1562). He was Vesalius' most famous student. Falloppio variously taught anatomy at Ferrara, Pisa and Padua and attacked the teachings of Galen more violently than many of his con-

temporaries. His contributions in the field of anatomy were numerous and outstanding. He verified many of Vesalius' observations pertaining to the heart and vessels and also demonstrated the coronary vessels by dissection. "Medici mutinensis observationes" was his outstanding work and was published in the year of his death, 1562. Falloppio described a nerve plexus in the heart and corrected the findings of Vesalius regarding the course of the cerebral arteries. Among other anatomic descriptions of Falloppio are the tubes which bear his name, the chorda tympani nerve, the semicircular canals and the circular folds of the small intestine.

Bartolommeo Eustachi (Eustachius) (1524–1574) was professor at the Collegia della Sapienza in Rome where in 1552 he completed a set of anatomic illustrations, "Tabulae anatomicae." They were the first anatomic plates made on copper and were said to surpass those in Vesalius' work. They remained in the Papal Library for 162 years but were finally released and published with commentaries by Lancisi in 1714. Eustachius described the pulmonary veins. He also discovered the eustachian tube, the thoracic duct, the adrenals and the abducens nerve. Eustachius gave the first accurate description of the uterus and described the cochlea, the muscles of the throat and the origin of the optic nerves. One of his detailed studies was concerned with the structure of the teeth including their nerve and blood supply.

Gabriele Falloppio (Fallopius).

Another celebrated Italian anatomist, Andrea Cesalpino (1519 or 1524–1603) (see special biography), was professor of medicine at Pisa and physician to Pope Clement VIII. He is a most important historic personality because a long standing bitter controversy has existed as to whether Cesalpino or Harvey was the true discoverer of the circulation. The Italian historians, particularly, are vehement in their contention that the priority of this important discovery belongs to Cesalpino. In a recent monograph on this subject Arcieri made the following impressive statement: "Unfortunately there is an unlimited number of historians, ever renowned, who elect themselves critics in the question, obviously without having performed the hard task of reading

all the Cesalpinian works." While some historians acknowledge that Cesalpino conceived the general idea of the circulation of the blood they contend that he presented no experimental evidence to this effect.

However, Arcieri denied this allegation and quoted directly and extensively from Cesalpino's works to the effect that his conclusions were based on detailed dissections, observations on the motions of the heart and vessels and on clear reasoning. Arcieri's monograph merits careful study. Corwin in a recent publication supported the Italian contention of Cesalpino's priority. Whatever the true facts may be there can be no question that Cesalpino's work was important and, together with previous and subsequent observations, finally removed many of the mysticisms pertaining to the heart and circulation.

Bartolommeo Eustachi (Eustachius).

Cesalpino's works included his "Quaestionum peripateticarum," 1571, and "Quaestionum medicarum," 1593. Among his observations was the recognition of a difference in both the structure and the function of the pulmonary artery and vein, a description of the origin, course, and size of the aorta and the vena cava, and recognition of a difference in the structure of the veins and arteries. He established the fact that communications exist between the portal veins and the vena cava, observed the reciprocal relation of cardiac contraction and vascular dilatation, and postulated an anastomosis between arteries and veins. These observations certainly indicate that Cesalpino was possessed of a remarkably clear idea of the general scheme of the circulation.

This portion of the sixteenth century produced still another illustrious Italian scientist. Hieronymus Fabricius ab Aquapendente (1537–1619), a great teacher, surgeon and anatomist, was the teacher of the famous William Harvey. Fabricius was appointed professor of surgery at Padua in 1565, and of anatomy in 1571. He studied the effect of ligatures on the limbs and historians are agreed that his precepts exerted an important influence on his celebrated pupil.

Harvey in his monumental work, "Exercitatio anatomica de motu cordis et sanguinis in animalibus," contended that Fabricius did not correctly grasp the function of the valves of the veins. Fabricius stated that the valves were placed in such a manner that their mouths were al-

ways directed toward the heart. He is said to have been the first to establish embryology on a practical basis although several other observations preceded his studies. In his work, Fabricius described the formation of the chick in the egg.

In surgery, Fabricius was cautious and avoided hazardous procedures. He described the technic for tracheotomy, thoracentesis and urethral surgery, and ligated arteries.

The list of celebrated Italian anatomists continues. Giulio Cesare Aranzio (1530–1589), professor of anatomy at Bologna, contributed particularly to knowledge of the anatomy of the fetus. He discovered the ductus arteriosus, a discovery often attributed to Botallo. Much documentary confusion exists regarding the identity of Botallo. Castiglioni asserted that while this name has been associated with the ductus arteriosus, Botallo is believed to have confused the foramen ovale with the ductus. History variously records Botallo's birth in 1530, the same year that other references indicate as the year of his graduation, and he is said to have been a student of Lanfranc who lived approximately three centuries earlier. With the evidence at hand it seems justifiable to credit Aranzio with the discovery of the ductus arteriosus.

Aranzio also discovered the ductus venosus of the fetus and the corpora arantii in the heart valves. Two years before his death, he demonstrated the reversal of the projected image on the retina of cattle.

Arcangelo Piccolomini (1525–1586), of Ferrara, an anatomist of the Roman Athenaeum, described the function of the valves of the jugular veins as well as of the veins of the extremities. He demonstrated that the arrangement of the valves was designed in such a manner as to prevent the reflux of blood to the head and to the dependent portions of the body. These observations appeared in his work, "Anatomicae praelectiones," published at Rome in 1586. Piccolomini also described the foramen ovale and the general conformation of the fetal heart.

Prosper Alpinus (1553–1617) practiced medicine in Cairo for many years. He made numerous important documentations of early Egyptian medicine. Alpinus wrote a two volume work, "The presages of life and death in diseases," which was translated by R. James of England in 1746. Alpinus described and discussed the three principal causes of the pulse, which he ascribed to the necessity of pulsation, the vital faculty or function and the subservience of the pulse to the faculty.

In the following record occurs the confirmation of the previous findings of Aranzio and Piccolomini. Giambattista Careano (1536–1606), of Milan, a student of the celebrated Fallopius, became professor of anatomy at Pavia. In 1593 he published a work dealing with the source of the vessels of the fetus and among these observations was a description of the ductus arteriosus and the foramen ovale. Careano was the first to give accurate descriptions of the ocular muscles and the lacrimal glands.

The first record dealing with the use of the single ligature in the treatment of peripheral aneurysm is that of Jacques Guillemeau (1550–1613). A student of Ambroïse Paré (1510–1590), he became a prominent surgeon, obstetrician and ophthalmologist. In 1594 Guillemeau applied a single ligature above the sac of an aneurysm of the brachial artery.

Garrison asserted that while Guillemeau was the first actually to perform the procedure, its employment had been suggested by the Byzantine, Aëtius (sixth century A. D.) of Amida.

Guillaume de Baillou.

In his obstetric work, Guillemeau recommended podalic version but was opposed to the use of cesarean section until after the death of the mother.

Guillaume de Baillou (1538–1616), a Paris graduate, was selected by Henry IV to be the personal physician to the Dauphin. He became dean of the Medical Faculty in 1580. Baillou was a student of Fernel. All of Baillou's works were published posthumously. He was an able clinician and wrote extensively on a great variety of medical subjects.

Baillou described palpitation of the heart as a manifestation of pericardial effusion in his work, "Consiliorum medicinalium libri II" (Venice, 1735). The following is a quotation from Major's "Classic descriptions of disease": "Besides these mentioned causes, inflammation, water contained in the sac of the heart, likewise if the sac contained within either a fluid putrid and smelling badly, or stones, it causes throbbing. . . ."

Baillou was one of the earliest epidemiologists and described whooping cough, diphtheria and rheumatic fever in his "Epidemiorum et ephemeridum libri duo, Opera omnia" (Venice, 1734). Baillou referred to whooping cough as "quinta" and differentiated between rheumatism and gout. He wrote an extensive glossary on Hippocratic terms, "Definitionum medicinalium liber," published in 1639.

SUMMARY

As one contemplates this century and a half of medical history it becomes evident that a true awakening of medical thought and endeavor occurred. While some false precepts and prohibitions of the preceding

and less enlightened era still prevailed, the spirit of scientific inquiry gradually expanded and was followed by constructive action. This intellectual revival was facilitated by certain important happenings. The papal edict, toward the close of the fifteenth century, permitting anatomic dissections on cadavers greatly influenced the remarkable progress made in this field, particularly by the Italian anatomists. The discovery of the printing press and the making of books was a potent force in the dissemination of knowledge and the interchange of scientific ideas among nations. This era, furthermore, witnessed the birth of true medical art which developed a completely new method of teaching. Little doubt exists that the rapid advances which occurred both in anatomic discovery and in teaching resulted in a large measure from this new method of graphic instruction.

Many hitherto unknown structures were described, named and identified and slowly the general pattern of the heart and circulation was evolved. While certain proof was still lacking, the main scheme of both the systemic and the pulmonary circulations was at least predicted. This in itself was monumental because all subsequent studies were by necessity based on a reasonably correct conception of this vital system. Knowledge of the finer details of the cardiovascular system, such as the cardiac valves, the valves of the veins, the course and distribution of vessels, and so forth, gradually evolved.

Embryology became an established science and the cardiovascular arrangements peculiar to the fetus were described and discussed. Pathologic anatomy became more mature although it did not flourish until the succeeding century. Malposition of the heart was recorded, fibrinous pericarditis and pericardial effusion were described and intracardiac thrombi were noted but misinterpreted. Aneurysms were recognized, were identified as true or false, and were associated with syphilis.

Physiologic progress was not notable although attempts were made to understand the function of organs and structures. Speculation on anatomic disclosures still prevailed. A few experiments were conducted dealing with the flow of blood, injection of water into arteries to observe their course, the use of artificial respiration in thoracotomy to maintain life, and the resuscitation of the nonbeating heart by means of bellows. The suggestion was made but not resolved, that valuable information could be acquired by estimating the weight of the blood and urine.

The Renaissance, while productive only in a limited sense, was nevertheless an important era in the evolution of medicine. Medical thought and inquisitiveness became kindled, and without undue interference were destined to play their role in the ultimate expansion of scientific endeavor and contribution. Medical education was a powerful force in this expansion and the era was blessed with a long line of brilliant and excellent teachers. It is important to note that during this period of

history, the majority of contributions came from the Italian and French schools of medicine.

REFERENCES

Krebs

Castiglioni, Arturo: A history of medicine. (Translated by E. B. Krumbhaar.) New York, Alfred A. Knopf, 1941, p. 370.
Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, p. 259.

Benedetti

Castiglioni, Arturo: Op. cit., p. 369.
Garrison, F. H.: Op. cit., p. 215.
White, P. D.: Heart disease. Ed. 3, New York, The Macmillan Company, 1944, p. 955.

Benivieni

Castiglioni, Arturo: Op. cit., p. 370.
Garrison, F. H.: Op. cit., p. 232.
Vierordt, Hermann: Geschichte der Herzkrankheiten. In Puschmann, Theodor: Handbuch der Geschichte der Medizin. Jena, Gustav Fischer, 1903, vol. 2, p. 633.
White, P. D.: Op. cit., p. 955.

Leonardo da Vinci

Arcieri, J. P.: The circulation of the blood and Andrea Cesalpino of Arezzo. New York, S. F. Vanni, 1945, p. 27.
Castiglioni, Arturo: Op. cit., pp. 410–417.
Garrison, F. H.: Op. cit., pp. 215–217.
Guthrie, D. J.: A history of medicine. Philadelphia, J. B. Lippincott Company, 1946, p. 135.
Herrick, J. B.: A short history of cardiology. Springfield, Illinois, Charles C Thomas, 1942, pp. 14–17, 207 and 208.
Peattie, D. C.: Leonardo da Vinci: The first modern. The Catholic World. 163: 137–143 (May) 1946.
Singer, Charles: A short history of medicine; introducing medical principles to students and non-medical readers. New York, Oxford University Press, 1928, pp. 83–84.

da Carpi

Castiglioni, Arturo: Op. cit., pp. 417–418.
Garrison, F. H.: Op. cit., p. 251.
White, P. D.: Op. cit., p. 955.

Linacre

Garrison, F. H.: Op. cit., pp. 195–196.
Herrick, J. B.: Op. cit., p. 13.
Osler, William: Thomas Linacre. Cambridge, University Press, 1908, 64 pp.

Paracelsus

Castiglioni, Arturo: Op. cit., pp. 445–450.
Garrison, F. H.: Op. cit., pp. 204–207.

Massa

Castiglioni, Arturo: Op. cit., p. 462.
Garrison, F. H.: Op. cit., p. 207.

Herrick, J. B.: Op. cit., p. 191.
Vierordt, Hermann: Op. cit., p. 633.

Vesalius

Arcieri, J. B.: Op. cit., pp. 51, 53, 55, 56, 70, 71 and 72.
Castiglioni, Arturo: Op. cit., pp. 418–425.
Garrison, F. H.: Op. cit., pp. 217–220.
Herrick, J. B.: Op. cit., pp. 4 and 208.
Singer, Charles: Op. cit., p. 89.
Singer, Charles: Some galenic and animal sources of Vesalius. J. Hist. Med. & Allied Sc. 1:6–24 (Jan.) 1946.
Willius, F. A.: Cardiac clinics. CXII. The historic development of knowledge relating to the coronary circulation and its diseases: introduction and the preharveian era. Proc. Staff Meet., Mayo Clin. 20:106 (Apr. 4) 1945.

Canano

Arcieri, J. P.: Op. cit., pp. 70 and 72.
Castiglioni, Arturo: Op. cit., p. 418.
Garrison, F. H.: Op. cit., p. 222.
White, P. D.: Op. cit., p. 955.

Guidi

Castiglioni, Arturo: Op. cit., p. 436.
Garrison, F. H.: Op. cit., p. 223.

Stephanus

Castiglioni, Arturo: Op. cit., p. 442.
Garrison, F. H.: Op. cit., p. 224.

Servetus

Arcieri, J. P.: Op. cit., pp. 49, 51–54, 66, 81 and 133–134.
Castiglioni, Arturo: Op. cit., p. 434.
Cumston, C. G.: The biography of Michel Servetus, the discoverer of the pulmonary circulation. Boston M. & S. J. 156:451–461 (Apr. 11) 1907.
Garrison, F. H. Op. cit., p. 220.
Herrick, J. B.: Op. cit., pp. 14, 18–22 and 25.
Osler, William: Michael Servetus. Bull. Johns Hopkins Hosp. 21:1–11 (Jan.) 1910.
Willius, F. A.: Cardiac clinics. CXIII. The historic development of knowledge relating to the coronary circulation and its diseases. II. Harvey and the seventeenth century. Proc. Staff Meet., Mayo Clin. 20:155–156 (May 16) 1945.

Fernel

Castiglioni, Arturo: Op. cit., p. 443.
Garrison, F. H.: Op. cit., pp. 196–197.
Herrick, J. B.: Op. cit., pp. 14, 21, 36 and 199.
Major, R. H.: Classic descriptions of disease; with biographical sketches of the authors. Ed. 2, Springfield, Illinois, Charles C Thomas, 1939, p. 485.

Paré

Castiglioni, Arturo: Op. cit., pp. 474–479.
Garrison, F. H.: Op. cit., pp. 224–226.
Herrick, J. B.: Op. cit., pp. 21, 34 and 199.
Major, R. H.: Op. cit., pp. 485–489.
Singer, Charles: Op. cit. (A short history of medicine), pp. 92–94, 162 and 247.

Sylvius

Arcieri, J. P.: Op. cit., p. 74.
Castiglioni, Arturo: Op. cit., p. 419.
Garrison, F. H.: Op. cit., pp. 218 and 222.
Herrick, J. B.: Op. cit., pp. 18 and 33.

Colombo

Arcieri, J. P.: Op. cit., pp. 15, 32, 47–49, 51–56, 66, 76, 81, 86, 109 and 133–134.
Castiglioni, Arturo: Op. cit., pp. 435–436.
Garrison, F. H.: Op. cit., p. 222.
White, P. D.: Op. cit., p. 955.

Fallopius

Castiglioni, Arturo: Op. cit., pp. 425–427.
Garrison, F. H.: Op. cit., pp. 191, 218 and 223.
Gross, Louis: The blood supply to the heart; in its anatomical and clinical aspects. New York, Paul B. Hoeber, 1921, pp. 1 and 30.
Herrick, J. B.: Op. cit., pp. 25 and 199.

Eustachius

Arcieri, J. P.: Op cit., pp. 117, 119 and 121.
Castiglioni, Arturo: Op. cit., pp. 427–428.
Garrison, F. H.: Op. cit., pp. 221–222.
Herrick, J. B.: Op. cit., p. 18.

Cesalpino

Arcieri, J. P.: Op. cit., 193 pp.
Castiglioni, Arturo: Op. cit., pp. 436–440.
Corwin, W. C.: William Harvey and the circulation of the blood. Proc. Staff Meet., Mayo Clin. 12:668–672 (Oct. 20) 1937.
Garrison, F. H.: Op. cit., p. 231.
Herrick, J. B.: Op. cit., pp. 25 and 29.
White, P. D.: Op. cit., p. 956.

Fabricius

Arcieri, J. P.: Op. cit., pp. 56, 59–60, 70, 72, 74–75, 81 and 115.
Castiglioni, Arturo: Op. cit., p. 473.
Garrison, F. H.: Op. cit., p. 223.
Herrick, J. B.: Op. cit., pp. 25 and 28.
Singer, Charles: Op. cit. (A short history of medicine), pp. 109–111.

Aranzio

Castiglioni, Arturo: Op. cit., pp. 427–428.
Garrison, F. H.: Op. cit., pp. 223 and 261.

Piccolomini

Arcieri, J. P.: Op. cit., pp. 77–79, 81 and 117.
Castiglioni, Arturo: Op. cit., p. 429.

Alpinus

Castiglioni, Arturo: Op. cit., p. 452.
Garrison, F. H.: Op. cit., p. 208.
Horine, E. F.: An epitome of ancient pulse lore. Bull. Hist. Med. 10:219–220 (July) 1941.

Carcano

Castiglioni, Arturo: Op. cit., p. 429.

Guillemeau

Castiglioni, Arturo: Op. cit., p. 483.
Garrison, F. H.: Op. cit., pp. 123 and 347.

Baillou

Castiglioni, Arturo: Op. cit., p. 470.
Garrison, F. H.: Op. cit., pp. 207–208.
Herrick, J. B.: Op. cit., pp. 37 and 191.
Major, R. H.: Op. cit., pp. 438–439.
Singer, Charles: Op. cit. (A short history of medicine), pp. 98 and 99.

4

THE SEVENTEENTH CENTURY

*Science commits suicide when it adopts a creed.**

THE SEVENTEENTH century was a stormy period in history; wars, religious rivalries and other disturbing forces retarded both scientific and cultural progress. The existent religious discord not only profoundly affected the lives and actions of individuals but likewise disrupted the political and economic status within nations and also between nations. Revolt against existing conditions became the catchword and science, trapped in the maelstrom of events, likewise showed its resentment. The Thirty Years' War, virtually decimating Germany, was not an event conducive to either scientific or cultural progress.

Both England and Holland attained their maritime supremacy at this time and the glorious Elizabethan age of ascendant English culture and science began. This was the age of Shakespeare, Milton, Newton, Francis Bacon, William Gilbert and Harvey, to mention only a few.

This era of medicine, owing to many antagonistic forces, became characterized by strong individualism and resulted in the development of many theories and systems. Many of the fallacious speculations and certain prohibitions of the previous eras still prevailed. Notwithstanding, some monumental works came into being, which in the case of medicine as a whole and in the field of the heart and circulation in particular, completely revolutionized medical thought and understanding and afforded subsequent workers the opportunity to proceed on correct premises.

It is clearly beyond the intent and scope of this volume to discuss the historic aspects of scientific societies; yet there is one which had its origin in this century and became famous as the years progressed through the efforts and achievements of its numerous illustrious members. Many of the celebrated members of this organization have been contributors to the history of cardiology, not only in the seventeenth century but also in the centuries to follow. Therefore, brief historical comment regarding the origin and development of the Royal Society of London seems appropriate.

Its beginning was inconspicuous but significant; a small group of young men formed a research club in Oxford, to hold weekly meetings. The average age of the members was thirty-four years. They met at the homes or in the rooms of the various members and their mutual interest

* Thomas Henry Huxley (1825–1895), quoted by Garrison, p. 14.

lay in natural philosophy. These young men of ambition and vision had wearied of the useless arguments dealing with religion, politics and the existent economic depression and decided to project their energies into productive channels. The little group frequently met at the lodgings of Dr. William Petty, because this dwelling housed an apothecary's shop where drugs and remedies were readily available for their investigations.

Eager to pursue a genuine investigative program and to inquire into the actual truth of matters, they resolved to pursue Nature rather than the written words of man. John Wallis (1616–1703), a member, who later became an eminent mathematician and wrote an important treatise on instruction of deaf-mutes, stated that the members confined themselves to philosophic inquiries dealing with physics, anatomy, geometry, astronomy, navigation, statics, mechanics and natural experiments.

Among the membership roster were such names as Robert Boyle, Robert Hooke, Seth Ward, Matthew Wren, Christopher Wren, Thomas Willis, Jonathan Goddard, Francis Glisson, George Ent, Charles Scarborough, William Petty and Christopher Merritt.

Robert Boyle (1627–1691), the great chemist and physicist, made intermediary contributions to the ultimate discovery of oxygen; Robert Hooke (1635–1703) performed pioneer studies in microscopy; Christopher Wren (1632–1723), the great architect, was also interested in medicine and illustrated Willis' book. Thomas Willis (1621–1675) made numerous contributions to knowledge of the brain and nervous system and was the discoverer of the circle of Willis; Francis Glisson (1597–1677) described the capsule of the liver, and George Ent was the close friend and executor of William Harvey. In addition to these were Charles Searborough, who later was to be physician to Charles II in his last illness; William Petty (1623–1687), who became Cromwell's First Physician to the Army of Ireland, and Christopher Merritt, who was later the first custodian of the medical library which William Harvey presented to the Royal College of Physicians about 1650.

This research club became unofficially known as the Oxford Philosophical Society and about 1658 the meetings ceased to be held in Oxford because a number of the members had moved to London. Contemporarily, in 1645 a small group of men had formed a similar organization in London which was alluded to as the "Invisible College." Attracted by mutual interests and bonds, the two clubs decided to merge and thus came into being the Royal Society of London. In 1662 Charles II bestowed the royal charter which was inscribed by the King as Founder, and James, the Duke of York, as Fellow.

The official journal of the Royal Society was established in 1664–1665 and was named the "Philosophical Transactions of the Royal Society." This was destined to be the medium of publication of important dis-

coveries and articles of innumerable eminent physicians and teachers, not only from England but also from many other countries. During these formative years, Robert Hooke was curator of experiments.

Before considering the strictly medical events of the seventeenth century it is of interest to note briefly that two famous astronomers and mathematicians utilized the timing of the pulse for their peculiar needs. As early as 1600, Johann Kepler (1571–1630), the great German astronomer, counted and utilized the pulse count in his astronomic observations. Later, Galileo Galilei (1564–1642) conceived the idea of using his own pulse count to test the regularity of the swing of a pendulum and then reversed the procedure to count the pulse by means of a pendulum.

Santorio Santorio (Sanctorius).

Others were also interested in devising instruments to bring about greater accuracy in recording body phenomena. Santorio Santorio (Sanctorius) (1561–1636), of Capodistria, was a professor at Padua and a clever inventor of medical instruments. He was the first seriously to apply quantitative determinations in preference to qualitative estimations. Sanctorius invented a clinical thermometer, an accomplishment also credited to Galileo. In 1625, Sanctorius devised a pulse clock or pulsilogium, which consisted of a weight suspended on a thread. The thread was held in the hand and the weight allowed to oscillate like a pendulum. The oscillations were increased in frequency as the thread was shortened and this maneuver was carried out until the weight oscillated to the frequency of the pulse. The free length of the thread was then read on an appended scale.

Sanctorius also devised an ingenious balance for determining the varying weights of an individual under different circumstances. He studied what he called "invisible perspiration."

WILLIAM HARVEY AND HIS WORK

The most outstanding and brilliant work of the seventeenth century was that of William Harvey (1578–1657) (see special biography). Born at Folkestone, he studied anatomy at Padua under the celebrated Hieronymus Fabricius of Aquapendente and received his diploma in

1602. He is generally recognized as the discoverer of the circulation of the blood although the formulation of the general concepts of pulmonary circulation had been made by Ibn an-Nafis (circa thirteenth century) and Michael Servetus (1553) and of the pulmonary and systemic circulations by Cesalpino (1571). History definitely records these previous contributions in the aforementioned chronologic order but even so, their effect on medicine was not profound nor enduring. Much confusion still prevailed because many erroneous speculations and fallacies of the past were still dominant in the minds of physicians. In contrast, Harvey's exposition did ultimately obtain universal approbation though at first such celebrities as Riolanus, Gassendi and Wormius refused to accept it. However, in the present advanced period of medical history it seems useless to squabble about remote priorities and it is therefore more fitting to credit properly all these great investigators who each shared in a great discovery.

Earlier physicians, as already mentioned, accepted the belief that a movement of the blood occurred but, like Galen, believed that this movement took place in the veins by a process of ebb and flow. Some still believed that the arteries contained air (spirits) while only the veins contained blood. The complete concept of the circulation of the blood had not been universally comprehended, although Arcieri insists that Cesalpino did grasp the general idea of this phenomenon. The liver, rather than the heart, was considered to be the central organ of the vascular system, and it was in the liver that the production of blood was said to occur. The belief existed that two kinds of blood were present; the one flowed from the liver to the right chambers of the heart and to the lungs and then returned to all parts of the body by the veins; the other flowed from the left chambers of the heart to the various parts of the body by the arteries. Furthermore, Galen's fallacious teaching that invisible pores in the septum of the heart existed was still widely accepted, and this concept permitted a small amount of blood from the right ventricle to trickle through to the left ventricle. No clear conception existed that the heart was a dynamic or propulsive organ designed primarily for the conveyance of blood from the heart and ultimately back to the heart. Even the muscular nature of the heart was a debatable issue and many of the early physicians considered the pulsations of the heart and the arteries to be the result of the alternate contraction and expansion of the air (spirits).

Harvey's findings dispelled all these fallacious and confused concepts and permitted all who were willing to understand, to grasp the correct basic concepts of the functions of the heart and circulation as a well-ordered and purposeful system. He proved that the contraction of the heart and not its dilatation is synchronous with the pulse, that the ventricles in their contraction squeeze out the contained blood and

propel it into the aorta and the pulmonary artery, that the pulse is produced by the arteries becoming filled with blood, that no invisible pores exist in the cardiac septum and that the only means whereby blood from the right side of the heart can reach the left side is through the pulmonary circulation. Harvey completed the demonstration of the circulation of the blood in his contention that the blood from the left side of the heart courses through the arteries, reaches the veins by small communicating vessels which he could not visualize but postulated, and is then returned to the heart. He demonstrated that both the arteries and the veins contain blood, that the movement of the blood occurs in a progressive and not in an undulating manner and that the functional center of the vascular system is the heart and not the liver.

Pierre Gassendi.

Harvey's work, "Exercitatio anatomica de motu cordis et sanguinis in animalibus," was published in Latin at Frankfurt am Main in 1628. Earlier notes, now in possession of the British Museum, indicate that Harvey was acquainted with the general facts concerning the circulation as early as 1616. No one can read Harvey's work and doubt his clear understanding of the function of the heart and circulation. While he lived before the age of adequate magnification, his clear logic permitted him to predict the existence of the capillary circulation. His contribution was the outgrowth of careful dissection, intelligent observation, experimentation (ligation of vessels) and sound reasoning. The eventual acceptance of Harvey's work dispelled the last fallacies of Galen, which had haunted the medical conscience for nearly fifteen centuries.

Without the realization of cause and effect, Harvey described what appears to be the first recorded instance of spontaneous rupture of the left ventricle in the famous case of the young Lord Montgomery. This report appeared in his "Exercitationes anatomicae de generatione animalium," published in 1660.

HARVEY'S CONTEMPORARIES AND SUCCESSORS

A prominent Italian physician, Fabrizio Bartoletti (circa 1630), recorded certain interesting clinical and pathologic correlations in his

work, "Methodus in dyspnoeam," Bononiae. He deseribed perieardial adhesions and fatty accumulations in the perieardium, uleeration of the heart (ulcerative endoearditis) and "ossifieation" of the aortie valves. Bartoletti also diseussed intraeardiae thrombi, whieh he, like others of his eontemporaries, believed to be eardiae polyps.

Robert Fludd (1574–1637) of England, an early advocate of inoeulation, made extensive observations on the pulse and its timing. His work, "Pulsus seu nova et areana pulsuum historia e saero fonte radiealiter extraeta, nec non medieorum ethnicorum dietis et authoritate comprobata," was published at Frankfurt in 1630. It was largely an aeeumulation of aneient data to whieh were added some personal observations.

An interesting observation eoncerning a eongenital eardiae defeet in an adult was reeorded by Pierre Gassendi (1592–1655) of Champtereier, Franee. He delved, but probably not too deeply, into anatomy, physics and astronomy. Gassendi found time to disagree violently with the diselosures and philosophies of many of his eontemporaries and predecessors. He refused to accept Harvey's work, attacked the teachings of Aristotle, opposed the philosophy of Robert Fludd and eriticized the metaphysical coneeptions of Descartes. Gassendi attributed the discovery of the circulation to one Fra Paolo Scarpi (1623), who is only mentioned casually if at all by medical historians.

Jean Riolan (Riolanus).

Among Gassendi's writings were observations on the formation of the fetus. In 1640, in collaboration with three other authors, the work, "De foetus formatione," was published. In this work was the deseription of the foramen ovale in an adult. This was not Gassendi's discovery but rather his observation of a postmortem examination which he had witnessed during the period that he was professor at Aix.

The first known reference to aspiration of the pericardium was that of Jean Riolan or Riolanus (1577–1657) of Paris. Professor of surgery at the University of Paris, he was the great dissenter of his era. Riolan was violently opposed to Harvey's teachings and tenaciously adhered to the previous concepts of Galen.

In 1649 Riolan advocated aspiration of the pericardium in cases in

which effusion occurred. He suggested trephining of the sternum as the approach to the pericardium. There is no record that Riolan practiced this procedure. This method was published in his work, "Encheiridion anatomicum pathologicum," 1653.

One of the earliest descriptions of a valvular lesion was recorded by Lazare Riviere (Riverius) (1589–1655), of Montpellier. He was a prominent physician, was greatly interested in the drug therapy of diseases and introduced the teaching of chemistry into the curriculum of the Montpellier school. Riverius was apparently the first to describe stenosis of the aortic valve (1646), which later appeared in his work, "Opera medica universa," Frankfurt, 1674.

Another component of the circulation was discovered by Jean Pecquet (1622–1674), of Dieppe, who was one of Harvey's stalwart supporters.

The Lesson in Anatomy of Dr. Tulp, by Rembrandt.

He discovered the thoracic duct, the receptaculum chyli and the structural union of the duct with the venous system. This work appeared in his "Experimenta nova anatomica," published in Paris in 1651. There were, however, contentions that this discovery had been made by Eustachius in 1568. The discovery of the lymphatic system was important and it significantly supplemented the already existing knowledge of the circulatory system.

In this period the Dutch anatomists reached eminence and included such celebrities as Pieter Paaw, Nicholas Tulp, Sebastian Egbert de Vriz and Regnier de Graaf. The Dutch masters used anatomists as subjects for their paintings and group portraits became popular. De Ghein, Rembrandt, Pietersz and deKeyser were but a few of the Dutch masters. Probably the most famous of all these anatomic group portraits is "The lesson in anatomy of Dr. Tulp," portraying the great anatomist with

seven of his students. Nicholas Tulp (Tulpius) (1593–1674) was professor of anatomy at Amsterdam. He described true polyps of the heart and distinguished them from postmortem thrombi, a subject that had been a controversial issue for many years.

An increasing interest was becoming evident among certain physicians in proving or disproving the correctness of their diagnoses. Benedetti and others during the Renaissance had conducted postmortem examinations but morbid findings had been chiefly disclosed during anatomic dissections. A brilliant German physician, Johann Jacob Wepfer (1620–1695), of Schaffhausen, performed many postmortem examinations and painstakingly recorded his findings. He was the first to establish definitely the causative relationship between cerebral hemorrhage and apoplexy, which appeared in his "Observationes anatomicae ex cadaveribus eorum quos sustulit apoplexia," Schaffhausen, 1658. This was an important contribution because the nature of apoplexy was greatly confused up to this time.


Johann Jacob Wepfer.

Marcello Malpighi (1628–1694) (see special biography), the founder of histology, variously served as professor of anatomy at Bologna, Pisa and Messina. He became interested in the use of the microscope, a new discovery (see the account of van Leeuwenhoek). According to the custom of the day many scientific discoveries were transmitted to friends and scientific contemporaries in the form of letters or epistles and later printed. For some years, Malpighi and Giovanni Borelli, professor of mathematics at Pisa, were close friends and freely exchanged scientific facts and data.

In 1661, Malpighi transmitted two letters to Borelli. In the first letter he described the vesicular character of the lung and demonstrated the manner in which the trachea branched into the bronchial tree, which in turn terminated in the pulmonary alveoli. In the second letter, Malpighi reported his histologic demonstration of the capillary anastomoses between arteries and veins. He was an adherent of Harvey's work and by actually demonstrating the capillary circulation he proved what Harvey had correctly predicted thirty-three years earlier.

According to Henker, evidence exists that the magnifying power of transparent mediums having convex surfaces was known at a very early date, because a convex lens of rock crystal was discovered by Layard among the ruins of the palace at Nimrud. Seneca also described hollow spheres of glass filled with water as being used for magnification. The precise gem cutting of the ancients could not possibly have been attained without the use of some method of magnification, and it may be assumed that these artisans made their own magnifiers. Convex glass lenses were first generally used to improve vision as spectacles. The spectaclemakers were not only the first to produce glass magnifiers, but they were also inventors of telescopes and the compound microscopes. During the period of the Thirty Years' War (1618–1648) the simple microscope was widely known, and Descartes in his "Dioptrique," published in 1637, described microscopes wherein a concave mirror was used together with a lens for illuminating the object. Antony van Leeuwenhoek, who also studied the capillary circulation some years after Malpighi's work, was apparently the first to succeed in grinding and polishing lenses of such short focal distances and perfect conformation as to make the simple microscope a more efficient instrument.

The early spectaclemakers insisted that a compound microscope—namely, one having two lenses so that small objects can be magnified—would never produce images as clear as those obtained by means of an instrument of the simple type, but this contention has proved to be fallacious.

About the end of the sixteenth century the compound microscope was invented. The inventors were probably the Middelburg lens grinders, Johann and Zacharias Jansen; the time, about 1590. The microscope had a negative eyepiece. It was not greatly improved until 1646, when Fontana described a microscope which had a positive eyepiece. This produced much better images and was, most likely, the type of instrument that Malpighi worked with. With this microscope he observed and studied the capillary circulation.

Another pioneer in microscopy was Robert Hooke (1635–1703), already mentioned as a charter member of the Royal Society of London. In 1665, he published his first work on the use of the microscope, "Micrographia: or some physiological descriptions of minute bodies made by magnifying glasses. With observations and inquiries thereupon." In studying the structure of cork, Hooke applied the term "cells" to the magnified units of the substance. This in reality was the origin of the cellular concept of animate organisms.

Hooke employed a condensing system for adding more light on the object being visualized and stated that he used a microscope which had three lenses. However, Hooke was aware of the fact that the simpler

the optical system, the better illumination and definition of objects was obtained. Therefore, in his observations, he frequently removed the middle lens and used only the eye lens and the objeet glass. Hooke's explanation for this proeedure rested on the knowledge that elearer vision resulted with only one refraction. The single lens type of magnifying apparatus was the type devised and used by Antony van Leeuwenhoek.

THE LATER SEVENTEENTH CENTURY

Another important anatomic exposition in this century was eontributed by a celebrated Danish anatomist. Niels Stensen (Nieholas Steno) (1638–1686), of Copenhagen, was a pupil of Thomas Bartholin, the great Danish anatomist who was responsible for integrating the general seheme of the lymphatie system. Stensen later attended the University of Amsterdam, where he worked under the supervision of Gerhard Blasius, but disagreements resulted in his departure and he eontinued his anatomic investigations at Leyden.

Niels Stensen.

Stensen proved the muscular nature of the heart in his famous work, "De musculis et glandulis observationum speeimen, eum epistolis duabus anatomieis," Amstelodami, P. le Grand, in 1664. This was a very significant contribution because the only other person to have considered the heart in the sense of a muscle was an unknown Alexandrian who wrote a treatise on the heart which is placed among the Hippocratic works. Stensen asserted that the heart substance is composed of only arteries, veins, nerves, fibers and membranes just as is the substance of other muscles.

As the second half of the seventeenth century is traversed, a keener and more intelligent inquiry into physiologic matters became apparent. This is personified in the work of Richard Lower (1631–1691), of Cornwall, a prominent physiologist and a successful practitioner of medicine. He was the first to perform direct transfusion of blood from one animal to another and predicted the feasibility of this procedure in man (1665). In his famous work, "Tractatus de corde," published in London in 1669, Lower made fundamental observations on the physiology of respiration.

After injecting dark venous blood into insufflated lungs he noted its subsequent bright red color and concluded that the change was due to the fact that the blood had absorbed some of the air passing through the lungs. He also demonstrated anastomoses between coronary arteries by experimentally injecting one artery from another.

Lower was interested in the mechanics of the heart and made observations of the changes accompanying systole. He considered the heart as a muscle. Lower observed the tamponade effect of pericardial effusion and discussed the limiting effect of pericardial adhesions on the movements of the heart.

Theodor Kerckring (1640–1693), of Amsterdam, contributed generously to anatomy. His anatomic work, "Spicilegium anatomicum," was published at Amsterdam in 1670. Kerckring was the first to recognize and describe the valvulae conniventes of the intestine, which still today are known by his name. He recognized postmortem thrombi within the chambers of the heart and contended that they were neither polyps nor worms, as some had believed.


Richard Lower.

An eminent Italian physician, anatomist and pathologist was Giovanni Guglielmo Riva (1627–1677), of Asti. He was Lancisi's teacher and was physician to Louis XIV and Pope Clement X. He founded a society of pathologists to which he made numerous addresses and also originated an anatomic museum. In 1670 Riva made notable contributions to the knowledge of the character and nature of aneurysms. He made numerous anatomic plates which were ultimately destroyed. Among them were plates depicting the entire lymphatic system. Riva (1668), like the French surgeon, Jean Baptiste Denis, attempted blood transfusion from animal to man with disastrous results. This brought about an edict from the Paris Faculty of Medicine prohibiting the procedure in France and later a papal bull prohibiting it in Italy.

Another early physiologic experiment related to the function of respiration was conducted by the Cornishman, John Mayow (1643–1679). Working with a gas which he obtained from niter and which he called nitro-aerial spirit, he noted that the dark venous blood be-

came red. Mayow did not realize that he had nearly discovered oxygen. He also described the function of the intercostal muscles as an aid to respiration and was the first to indicate the muscles of the body as the seat of animal heat. His work, "Tractatus quinque," appeared in 1674. Mayow also described dilatation of the left auricle and of the right ventricle in mitral stenosis.

Jan Swammerdam (1637–1680) was an outstanding Dutch biologist and physiologist who ultimately extended his investigations into the field of medicine. He was fundamentally a microscopist. Unfortunately, Swammerdam's career was cut short by insanity and he died at the premature age of forty-three years. He was the first to see and describe the erythrocytes in the blood of animals (1658) and was an early investigator of arterial injections. His experiments included the injection of materials with low melting points (wax) to enable him to study the finer tributaries and anastomoses of vessels.

John Mayow.

Swammerdam studied the movements of the heart, lungs and muscles by primitive plethysmographic methods. These experiments revealed that a muscle does not increase its bulk during contraction, contrary to the belief that was prevalent at the time and was found particularly in the teaching of Borelli. Swammerdam contended that no substance was brought to the muscle by the nerves and that the concept of a "nervous fluid" or *succus nerveus* was fallacious. He applied the same reasoning to the heart muscle (1677). His "Historia insectorum" was published in 1669 and his "Bijbel der natuur" was published after his death by Boerhaave in 1737.

Théophile Bonet (Bonetus) (1620–1689), of Paris, was a brilliant clinician and careful observer, always interested in the correctness or error of clinical diagnosis. He collected and analyzed all available postmortem records up to 1679 in his famous work, "Sepulchretum sive anatomia practica ex cadaveribus morbo de natis," published in Geneva in 1679 and 1706. Among the many cases recorded was that of sudden death in a patient with calcareous stenosis of the aortic valve and the case of an obese, middle-aged poet who died within a few minutes

following "distress in breathing." The latter instance may well have been a death resulting from coronary disease.

In the same period of the seventeenth century, Giovanni Alfonso Borelli (1608–1679), of Pisa, made certain deductions pertaining to the physiology of muscles. He was primarily a mathematician but became interested in biologic phenomena, largely through the influence of his friend Malpighi. Borelli had studied under the celebrated Galileo. He was a protagonist of Harvey's doctrines. Borelli became interested in the physiology of muscles, including heart muscle, and concluded that the contracting muscle increased its bulk by virtue of a fermentative process occurring in the muscle. His concept included the discharge of a fluid, *succus nerveus,* by the nerve supplying the muscle. This work appeared in his "De motu animalium" (1680–1681) although Jan Swammerdam had disproved his hypothesis three years earlier.

Théophile Bonet (Bonetus).

Lorenzo Bellini (1643–1704), who became professor of medicine at Pisa, was a student of Borelli and Redi. His interests were chiefly centered about physiology and pathology. Bellini's most outstanding work consisted of his demonstration of the structure of the kidney, "De structura renum," which appeared in 1662. He described calcification of the coronary arteries in his "De morbis pectoris," which appeared early in the succeeding century (1703). Bellini further studied the use of phlebotomy in clinical medicine and wrote an extensive treatise on the importance of studying the pulse and the urine in both health and disease. This work, "De urinis et pulsibus," appeared in 1683.

An ingenious character of this period was Antony van Leeuwenhoek (1632–1723), of Delft. He was an untutored, modest burgher who was the custodian of the city hall in his community. No commentary on the history of medicine would be complete without the inclusion of this remarkable man. Van Leeuwenhoek became interested in the science of magnification and devoted his spare time to the creation of the single biconvex lens microscope. He constructed the instruments, ground the lenses and is said to have possessed 247 microscopes and 419 lenses.

Many of his instruments were superior to the compound microscopes of his era and one of the microscopes still preserved at Utrecht has a magnification of nearly 200 diameters. While van Leeuwenhoek was not the originator of magnification, his improvements and persistent observations place him in a position of outstanding importance in early microscopic investigation.

Regnier de Graaf, also a resident of Delft, became greatly interested in van Leeuwenhoek's work and encouraged him in his investigations. De Graaf was a scientist in his own right and the discoverer of the graafian follicle, was a corresponding member of the Royal Society of London and urged van Leeuwenhoek to communicate his observations to the Society.

Giovanni Alfonso Borelli.

Van Leeuwenhoek's microscopic studies covered a broad field and among his contributions was a treatise, "On the circulation of the blood in fishes," (Translation) which appeared in the Philosophical Transactions of the Royal Society. In this communication, originally published in 1708, he expressed his weird conception of the pulse in stating that pulsations occurred in the veins and not in the arteries.

Earlier, van Leeuwenhoek had confirmed Malpighi's discovery of the capillary circulation, had observed the erythrocytes in blood but had mistaken them for fat cells, had been the first to observe and describe the leukocytes and also had been the first to reveal the fibrillar structure of muscles. Many of van Leeuwenhoek's observations appeared in his work, "Ontledingen en Ontdekkingen," Leyden, in 1696.

An interesting but not important record exists in the instance of Richard Wiseman (1622–1676), a skillful English surgeon. Among his writings was an account of aneurysm. In discussing its causes he stated that the "impetuosity of the Blood" was greater than the artery could sustain. In considering the causes of increased "impetuosity" of the blood Wiseman discussed the point that more blood was present than the vessel could withstand but admitted that this condition was rare because more commonly excessive blood escaped by way of the nose, the lungs, the brain (apoplexy), the stomach, the guts and the anus. More

commonly the quality of the blood was altered, either being "too sharp or thin, erodes the vessel; or, being highly fermented by other causes, burst through all." He also discussed external causes of aneurysm such as puncture caused by sharp weapons. The signs of aneurysm were considered and he concluded that all aneurysms were difficult to cure. This work appeared in "Eight chirurgical treatises" (III Ed., London, 1696).

In an experimental study, Pierre Chirac (1650–1732), a prominent French investigator, recorded what was probably the first attempt to study the effect of ligation of a coronary artery in the dog. In his work,

Antony van Leeuwenhoek.

Richard Wiseman.

"De motu cordis adversaria analytica," Monspelii, 1698, he concluded that the procedure produced cardiac standstill.

SUMMARY

The outstanding accomplishment of this century of medical progress was without a doubt Harvey's demonstration of the true nature of the anatomy and basic physiologic principles of the heart and circulation. However, history records many other important personalities whose contributions were important in the gradual clarification of some of the mysteries of the heart and circulation and their diseases. Important supplementary anatomic contributions were made in this century, notably the demonstration of the lymphatic system, the receptaculum chyli, the thoracic duct and its union with the venous system. Histology

became an established science and in this field several notable discoveries occurred. The erythrocytes were visualized and described for the first time, the structure of the lung and other viscera was demonstrated and the capillary circulation was proved. The muscular structure of the heart became a proved reality.

Physiology came into its own and the first concerted efforts to solve the problems of respiration were made. The physiology of muscles was investigated, arterial injections were made in order to study the finer ramifications of the vessels and ligation of the coronary arteries in the dog was performed.

An ever-increasing interest was manifested in the correlation of clinical symptoms and postmortem findings. Observations regarding the significance and clinical demonstration of cardiac enlargement appeared together with the recognition of congestive heart failure and concepts regarding its mode of production and its relation to pulmonary congestion, pulmonary edema and hydrothorax. The tamponade effect of pericardial effusion was postulated and the effects of pericardial adhesions in limiting the activity of the heart were described. The persistence of the foramen ovale in an adult was recorded.

The attempt at more precise pulse counting was made by the introduction of a pulse clock.

Spontaneous rupture of the heart, ulceration of the endocardium and ossification of the cardiac valves and coronary arteries were described. The differentiation between postmortem intracardiac thrombi and polyps was achieved and the relation of cerebral hemorrhage to apoplexy was established.

The seventeenth century, in spite of its handicaps, was a period of notable achievement.

REFERENCES

Sanctorius

Arcieri, J. P.: The circulation of the blood and Andrea Cesalpino of Arezzo. New York, S. F. Vanni, 1945, pp. 106 and 107.

Castiglioni, Arturo: A history of medicine. (Translated by E. B. Krumbhaar.) New York, Alfred A. Knopf, 1941, pp. 536-537.

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, p. 260.

Herrick, J. B.: A short history of cardiology. Springfield, Illinois, Charles C Thomas, 1942, pp. 14, 24 and 33.

Singer, Charles: A short history of medicine; introducing medical principles to students and non-medical readers. New York, Oxford University Press, 1928, p. 108.

Vierordt, Hermann: Geschichte der Herzkrankheiten. In Puschmann, Theodor: Handbuch der Geschichte der Medizin. Jena, Gustav Fischer, 1903, vol. 2, p. 645.

Weller, C. V.: Antony van Leeuwenhoek. Ann. Int. Med. 6:573-581 (Oct.) 1932.

Harvey

Arcieri, J. P.: Op. cit., 193 pp.
Castiglioni, Arturo: Op. cit., pp. 515–520.
Garrison, F. H.: Op. cit., pp. 246–249.
Harvey, William: Exercitatio anatomica de motu cordis et sanguinis in animalibus. Francofurti, G. Fitzeri, 1628, 72 pp.
Herrick, J. B.: Op. cit., p. 208.
Power, D'Arcy: William Harvey. London, T. F. Unwin, 1897, 283 pp.
Singer, Charles: Op. cit., pp. 32, 103, 111–115 and 135.
Smith, P.: A history of modern culture. New York, Henry Holt & Co., Inc., 1930, vols. 1 and 2, 1375 pp.
Vierordt, Hermann: Op. cit., pp. 606, 632 and 634.
White, P. D.: Heart disease. Ed. 3, New York, The Macmillan Company, 1944, pp. 147–148.
Willis, Robert (Translator): The works of William Harvey, M.D. London, The Syndenham Society, 1847, 624 pp.
Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors. St. Louis, C. V. Mosby Company, 1941, pp. 11–79.

Bartoletti

Vierordt, Hermann: Op. cit., pp. 634 and 642.

Fludd

Castiglioni, Arturo: Op. cit., p. 450.
Guthrie, Douglas: A history of medicine. Philadelphia, J. B. Lippincott Company, 1946, p. 158.
Horine, E. F.: An epitome of ancient pulse lore. Bull. Hist. Med. 10:230 (July) 1941.

Gassendi

Arcieri, J. P.: Op. cit., p. 75.
Castiglioni, Arturo: Op. cit., p. 519.
Tallmadge, G. K.: Pierre Gassendi and the *Elegans de septo cordis pervio observatio*. Bull. Hist. Med. 7:429–457 (May) 1939.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 81–85.

Riolan

Ballance, Charles: The surgery of the heart. Lancet. 1:1–5 (Jan. 3); 73–79 (Jan. 10); 134–139 (Jan. 17) 1920.
Castiglioni, Arturo: Op. cit., p. 519.
King, E. S. J.: Surgery of the heart. Baltimore, Williams & Wilkins Co., 1941, pp. 566 and 579.
Matas, Rudolph: Surgery of the vascular system. In Keen, W. W.: Surgery; its principles and practice. Philadelphia, W. B. Saunders Company, 1909, vol. 5, chap. 70, pp. 17–350.

Riverius

Castiglioni, Arturo: Op. cit., p. 560.
Gibson, G. A.: Diseases of the heart and aorta. New York, The Macmillan Company, 1898, p. 473.
Major, R. H.: Classic descriptions of disease; with biographical sketches of the authors. Ed. 2, Springfield, Illinois, Charles C Thomas, 1939, p. 559.

Pecquet

Arcieri, J. P.: Op. cit., pp. 117, 121 and 134.
Castiglioni, Arturo: Op. cit., p. 521.
Neuburger, Max: Einleitung. In Puschmann, Theodor: Handbuch der Geschichte der Medizin. Jena, Gustav Fischer, 1903, vol. 2, pp. 3–154.

Tulp

Castiglioni, Arturo: Op. cit., pp. 531–532.
Garrison, F. H.: Op. cit., pp. 272 and 283.
Guthrie, Douglas: Op. cit., p. 194.
Herrick, J. B.: Op. cit., p. 37.
Vierordt, Hermann: Op. cit., pp. 633–634 and 657.

Wepfer

Castiglioni, Arturo: Op. cit., p. 535.
Garrison, F. H.: Op. cit., p. 271.
Major, R. H.: Op. cit., pp. 512–515.
Vierordt, Hermann: Op. cit., p. 606.

Malpighi

Arcieri, J. P.: Op. cit., pp. 70, 117, 122, 124, 133 and 134.
Castiglioni, Arturo: Op. cit., pp. 522–524.
Foster, Michael: Lectures on the history of physiology during the sixteenth, seventeenth and eighteenth centuries. Cambridge, University Press, 1901, 310 pp.
Garrison, F. H.: Op. cit., pp. 255–256.
Guthrie, Douglas: Op. cit., pp. 186–189 and 198.
Henker, Otto: Microscope. The Encyclopedia Britannica. Ed. 11, Cambridge, England, University Press, 1911, vol. 18, pp. 392–407.
Herrick, J. B.: Op. cit., pp. 28, 31, 38 and 47.
Singer, Charles: Op. cit., pp. 116–120 and 302.
Vierordt, Hermann: Op. cit., pp. 626, 634 and 636.
Weller, C. V.: Op. cit., pp. 573–584.
White, P. D.: Op. cit., pp. 165–166.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 87–97.
Young, James: Malpighi's "De Pulmonibus." Proc. Roy. Soc. Med. (Section of the History of Medicine). 23(pt. 1):1–11 (Oct. 2) 1929.

Stensen

Arcieri, J. P.: Op. cit., p. 168.
Castiglioni, Arturo: Op. cit., pp. 520 and 524.
Garrison, F. H.: Op. cit., pp. 265–266.
Lutz, J. G.: Nicholas Steno. M. Library & Hist. J. 2:166–182, 1904.
Miller, W. S.: Niels Stensen. Bull. Johns Hopkins Hosp. 25:44–51 (Feb.) 1914.
Stensen, Niels: De musculis et glandulis observationum specimen, cum epistolis duabus anatomicis. Amstelodami, P. le Grand, 1664, 90 pp.

Lower

Castiglioni, Arturo: Op. cit., pp. 520, 524, 534 and 552.
Franklin, K. J.: The work of Richard Lower (1631–1691). Proc. Roy. Soc. Med. 25 (pt. 1):113–118 (Dec. 2) 1931.
Garrison, F. H.: Op. cit., p. 250.
Guthrie, Douglas: Op. cit., pp. 187–188.
Herrick, J. B.: Op. cit., pp. 37 and 209.
Major, R. H.: Op. cit., pp. 439–441.
Vierordt, Hermann: Op. cit., p. 634.
Willius, F. A.: Cardiac clinics. CXIII. The historic development of knowledge relating to the coronary circulation and its diseases. II. Harvey and the seventeenth century. Proc. Staff Meet., Mayo Clin. 20:156 (May 16) 1945.
Willius, F. A. and Keys, T. E.: Op. cit., p. 102.

Kerckring

Castiglioni, Arturo: Op. cit., p. 524.
Garrison, F. H.: Op. cit., p. 250.
Vierordt, Hermann: Op. cit., p. 634.
White, P. D.: Op. cit., p. 956.

Riva

Arcieri, J. P.: Op. cit., pp. 121, 122 and 134.
Castiglioni, Arturo: Op. cit., p. 521.

Mayow

Castiglioni, Arturo: Op. cit., pp. 542 and 583.
Garrison, F. H.: Op. cit., pp. 268–269.
Gibson, G. A.: Op. cit., p. 694.
Herrick, J. B.: Op. cit., pp. 36–38 and 110.
Singer, Charles: Op. cit., pp. 126, 151–152 and 189.
White, P. D.: Op. cit., p. 956.

Swammerdam

Castiglioni, Arturo: Op. cit., pp. 512 and 520.
Garrison, F. H.: Op. cit., pp. 253–254.
Herrick, J. B.: Op. cit., p. 21.
Singer, Charles: Op. cit., pp. 121–122.
Willius, F. A. and Keys, T. E.: Op. cit., p. 107.

Bonet

Garrison, F. H.: Op. cit., pp. 272 and 354.
Herrick, J. B.: Op. cit., pp. 52 and 202.
White, P. D.: Op. cit., pp. 627–628.
Willius, F. A.: Cardiac clinics. CXIV. The historic development of knowledge relating to the coronary circulation and its diseases: the eighteenth century. Proc. Staff Meet., Mayo Clin. 20:327 (Sept. 5) 1945.
Willius, F. A. and Keys, T. E.: Op. cit., p. 174.

Borelli

Arcieri, J. P.: Op. cit., pp. 106, 112 and 122.
Castiglioni, Arturo: Op. cit., pp. 537–538.
Garrison, F. H.: Op. cit., p. 258.
Guthrie, Douglas: Op. cit., pp. 197–198.
Herrick, J. B.: Op. cit., p. 33.
Singer, Charles: Op. cit., pp. 39, 129 and 131.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 90 and 92–97.

Bellini

Castiglioni, Arturo: Op. cit., p. 525.
Herrick, J. B.: Op. cit., p. 37.

Van Leeuwenhoek

Castiglioni, Arturo: Op. cit., pp. 511 and 528–530.
Dobell, Clifford: A protozoological bicentenary: Antony Van Leeuwenhoek (1632–1723) and Louis Joblot (1645–1723). Parasitology. 15:308–319 (Sept.) 1923.
Garrison, F. H.: Op. cit., pp. 254–255.

de Graaf, Regnerus: Some observations made by a microscope, contrived by M. Leewenhoek in Holland. Phil. Tr. Roy. Soc., London. 2(abridged):66–67, 1809.
Leuwenhoeck: On the circulation of the blood in fishes, etc. Phil. Tr. Roy. Soc., London. 5(abridged):461–464, 1809.
Nuttall, G. H. F.: Notes bearing on Leeuwenhoek, Redi, Linnaeus, DeGeer, Rudolphi, Müller, Leidy, Owen, Jenner, Kircher and Boyle, whose portraits have appeared in *Parasitology, Vol. XIII* (portrait plates I–XI). Parasitology. 13:398–400 (Nov.) 1921.
Plimmer, H. G.: The president's address: "Bedellus immortalis." J. Roy. Micr. Soc. 33:121–135, 1913.
Singer, Charles: Op. cit., pp. 39 and 118.
Weller, C. V.: Op. cit., pp. 573–584.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 115–123.

Wiseman

Castiglioni, Arturo: Op cit., p. 388.
Garrison, F. H.: Op. cit., pp. 276, 288 and 293.
Major, R. H.: Op. cit., pp. 490–491.

Chirac

Gross, Louis: The blood supply to the heart; in its anatomical and clinical aspects. New York, Paul B. Hoeber, 1921, p. 78.
Herrick, J. B.: Op. cit., p. 209.
Willius, F. A.: Op. cit. (Cardiac clinics. CXIII), p. 156.

5

THE EIGHTEENTH CENTURY

*Man can learn nothing unless he proceeds from the known to the unknown.**

In the eighteenth century medicine and other sciences became still more emancipated from the previously existent and still prevailing prohibitions and restrictions. The greater freedom of medical thought and initiative influenced this century of development both favorably and unfavorably. Theories and individual systems, already operative in the preceding century, flourished; medical literature increased greatly, both for good and for bad; so that Garrison was led to refer to this period as one of retrogression. While considerable knowledge had been acquired during the brilliant era of the Renaissance and the seventeenth century, it was to a great extent at loose ends and there existed an urgent need for classification and clarification.

It was the precise and orderly Linnaeus who initiated the new order of classification, in both botany and medicine. Inventive genius asserted itself in the realm of science and bore fruit in such celebrities as Cavendish, Priestley, Lavoisier, Galvani, Volta, Fahrenheit, Celsius, Watt, Fulton and others.

The practice of medicine became popular and the number of physicians increased significantly although in this more ample medical array only a limited number of outstanding physicians were evident. These outstanding men, however, contributed generously and significantly to the advancement of medicine and related sciences during their century.

One of the outstanding clinicians who bridged both the seventeenth and eighteenth centuries was Giorgio Baglivi (1668–1706) who died at the premature age of thirty-eight years. He was a student of the celebrated Malpighi and toward the close of the seventeenth century was appointed professor of anatomy at Rome, the position held by the great Eustachius a century earlier. When only twenty-eight years old Baglivi wrote his famous work, "De praxi medica," wherein he summarized his own extensive knowledge and experience and described the general status of medicine at the time. He was an inspiring teacher and established an extensive practice.

Baglivi was interested in physiologic correlations and conceived the human body and its essential functions as a machine, composed of

* Claude Bernard (1813–1878), cited by Garrison, p. 14.

many smaller machines. He compared the teeth to scissors, the stomach to a flask, the thorax to bellows, the heart and blood vessels to a pump and hydraulic system and so forth. He was one of the pioneer exponents of bedside medical instruction and stressed the principles of reasoning and observation. Baglivi also advocated specialization in medical practice. To his students he stressed the philosophy that the best book of medical knowledge is the recitation of the patient's symptoms.

Baglivi conducted experiments in the physiology of muscles and was the first to recognize and distinguish the differences between smooth and striated muscle (1700). The importance of this discovery with regard to the heart is obvious. He recorded classic descriptions of cardiac failure and asthma and studied the effects of ligation of arteries and veins while working with Malpighi at Bologna. Baglivi cut the vagi in the neck of a dog and observed that the animal was unable to bark and had periodic dyspnea and vomiting. It died on the twelfth day. He believed that these phenomena occurred because the union between the "vital spirit" and the heart had been severed. Baglivi performed many postmortem examinations. Among his observations were arteriosclerosis of the cerebral arteries and calcification of the pericardium described as "of a heart invested in a mortar sheath."

Giorgio Baglivi.

It fell to Baglivi's lot to record the medical history and to perform the postmortem examination of his teacher, Malpighi, who died as the result of a massive cerebral hemorrhage. This account was published in "The practice of physick," London, 1694.

One of the earliest records concerning the use of palpation in the diagnosis of cardiac disease was that of Francesco Ippolito Albertini (1662–1738). He was born near Bologna and was one of the most brilliant physicians of the early part of the eighteenth century. Albertini was a pupil of Malpighi and a contemporary and personal friend of Valsalva. His most outstanding work, "De affectionibus cordis," appeared in 1726. Albertini advocated and practiced the correlation of symptoms of disease with pathologic findings and utilized inspection and palpation to good advantage. He was particularly interested in de-

tecting enlargement of the heart as indicative of disease of the organ and employed palpation to locate the position of the apex beat.

Albertini related pains in the arms and shoulders to heart disease and emphasized the importance of dyspnea as a symptom. He described pulmonary edema and explained it as being the result of impaired circulation in and through the heart. He further ascribed dyspnea to congestion of the lungs and contended that its progression eventuated in hydrothorax. Albertini differentiated pulmonary congestion and pulmonary edema from hydrothorax. In cases of pericardial effusion he declared that the excursions of the heart were diminished and the apex pulsation became indistinct or disappeared.

Francesco Ippolito Albertini.

While Carolus Drelincourt (1633–1697), of France, lived in the preceding century, his contribution did not appear until nearly a century after his death. He, like Bellini before him, described calcification of the coronary arteries although he apparently did not appreciate the clinical significance of the findings. This observation was not recorded until 1770 when it appeared in a subsequent edition of the "Boneti sepulchretum."

Greater interest became manifest in correlating clinical symptoms with postmortem findings and descriptions of pathologic abnormalities of the heart became more lucid and intelligent. William Cowper (1666–1709) of London, the teacher of the celebrated English surgeon, William Cheselden, was the object of a bitter controversy when he allegedly plagiarized Bidloo's anatomic illustrations. This occurred when Cowper published his "Anatomy of human bodies," Oxford, in 1698. Godfrey Bidloo, the famous Dutch anatomist, had published his work, "Anatomia corporis humani, centum et quinque tabulis ad vivum delineatis," Amsterdam, in 1685. All but nine of the plates in Cowper's book were identical to those of Bidloo. In spite of this scandal, however, Cowper retained his professional and popular prestige.

Earlier he had published a work on the muscles, "Myotonia reformata or a new administration of the muscles of the human bodies." Cowper was the first to describe aortic insufficiency and one of the illustrations of this work demonstrates a typical example of stenosis of the aortic

valve. These observations appeared in his paper, "Of ossifications or petrifactions in the coats of arteries, particularly in the valves of the great artery." He also described the periurethral glands in the male which are still known as Cowper's glands, although he was not the first to describe them. The first description of these glands was recorded by Jean Mery (1645–1722) in 1684.

Raymond Vieussens (1641–1716), professor at Montpellier, was one of the leading contributors in the field of cardiology during the eighteenth century. His observations were remarkably accurate and carefully recorded. Many of his observations were published in his work, "Traité nouveau de la structure et des causes du mouvements natural du coeur," Toulouse, 1715. He described the position, structure and pathologic changes of the heart. Vieussens was the first to describe the structure of the left ventricle correctly and to describe the course of the coronary arteries, the valve of the large coronary vein and the coronary sinus. The idea that the coronary vessels have direct communication with the chambers of the heart was also advanced by Vieussens in 1705. He discussed the back pressure phenomena in mitral stenosis and described the resulting symptoms. He contended that cyanosis was not necessarily dependent on the admixture of venous and arterial blood and thus conceived the idea of anoxia.

William Cowper.

Vieussens further noted the significance of pericardial adhesions in relation to the restriction of cardiac activity and function and called attention to the relationship of asthma and hydrothorax to heart disease (1672–1676). He described the diagnostic features of pericardial effusion. In 1695 Vieussens, while discussing aortic insufficiency, commented on the peculiar water-hammer character of the pulse attending this valvular defect. He described mitral stenosis and its pathologic features in 1705. Vieussens is credited with making the first diagnosis of thoracic aneurysm during the life of the patient.

He also contributed to knowledge of the anatomy of the nervous system and among various observations in his "Neurologia universalis," 1685, described the centrum ovale in the brain. Vieussens further de-

scribed the structure of the ear and discussed the fermentative action of saliva.

The most brilliant Italian physician of this century was Giovanni Maria Lancisi (1654–1720), of Rome, who was a student of the celebrated Riva. His contributions to knowledge relating to the heart were numerous and important. Lancisi systematically collected postmortem observations and correlated them with clinical symptoms and signs. In 1707 he published his famous work, "De subitaneis mortibus," which dealt with the causes of sudden death. During the preceding year an unusual number of sudden deaths had occurred among the Roman populace and had created intense public anxiety. In this work Lancisi emphasized the important role played by cardiac enlargement in sudden death and he mentioned calcified coronary arteries as a cause of enlargement of the heart. He was also aware of the symptoms of the disorder later to be known as "angina pectoris" and their relation to sudden death.

Raymond Vieussens.

In an interesting experimental investigation Lancisi injected mercury into the coronary arteries and observed that it appeared in the chambers of the heart. This observation led him to speculate that the injected material escaped through venous channels. This contribution appeared posthumously in "De motu cordis et aneurysmatibus" (opus posthumum, 1728).

Lancisi related sudden death to structural changes in the heart and related syncope to nervous affections of that organ. He differentiated cardiac hypertrophy from dilatation and described valvular vegetations and calcification of the cardiac valves. In discussing the causes of cardiac enlargement he emphasized the effect of mechanical barriers resulting from both arterial and valvular disease, such as narrowing of valvular orifices.

Lancisi recognized that distention of the veins of the neck is associated with dilatation of the right chambers of the heart and he discussed regurgitation of blood at the tricuspid valve. He was the first to describe syphilis of the heart and wrote extensively on aneurysms, discussing their causes and distinguishing various types. It is of interest to note that

Lancisi appears to be the first to mention the hereditary tendency to cardiac disease. He asserted that the tendencies are transmitted from parent to child. He also noted and stressed the clinical importance of obliterative pericardial adhesions.

A provincial English physician of Staffordshire and Lichfield, Sir John Floyer* (1649–1734), was possessed of considerable inventive genius. He invented and devised a pulse watch designed to run precisely one minute and published a description of this under the title of the "Physician's pulse watch" in 1707. This was a great accomplishment because mechanical difficulties had not yet permitted the construction of a twenty-four-hour watch and the second hand of a watch had not yet been devised. Thus, a watch devised to run for precisely one minute permitted the pulse to be counted with great accuracy.

Giovanni Maria Lancisi.

Floyer wrote the first treatise on diseases of the aged, which undoubtedly represented the first contribution pertaining to geriatrics, "Medicina gerocomica," 1724.

In this same period of the eighteenth century, a German, Friedrich Hoffmann (1660–1742), of Halle, contributed to cardiology. A curious personality, he personified a peculiar mixture of the astute clinical observer, of a therapeutic enthusiast and of a mystic. His basic concept of medicine was centered about the belief that a mysterious fluid, acting through the nervous system, regulated the tonus of muscles. Hoffmann ascribed acute diseases to tonic or spasmodic states and chronic diseases to atonic states. He was an active therapeutist and the originator of the still existent Hoffmann's anodyne (spiritus aetheris compositus). Hoffmann also believed in evil spirits as causes of disease.

In 1707 he described convulsive asthma associated with dropsy and speculatively related these phenomena to the heart. In his work, "Operum omnium physico-medicorum supplementum secundum in tres partes distributum," Genevae, frates de Tournes, 1753, Hoffmann described the syndrome of angina pectoris without ascribing a name or a

* According to Joseph Wood Krutch in his volume "Samuel Johnson," Sir John Floyer was the physician who recommended to Johnson's parents that the boy be sent to be touched for the "king's evil."

cause to the symptoms. The patient was a man who suffered from pain and a sense of oppression in the precordial region, radiating in all directions and especially to the arms.

Another interesting and important investigation dealing with the coronary circulation was conducted by Adam Christianus Thebesius (1686–1732). These experiments were published in his work, "Disputatio de circulo sanguinis in corde," Lugdunum Batavorum, in 1708. In these investigations he injected materials into the coronary vessels and observed their passage into the chambers of the heart through small orifices in the endocardium. Thebesius knew of Vieussens' experiments and referred to them in his work.


Sir John Floyer.

Thebesius was of the opinion that these sinuses were connected only with the coronary veins. This sinusoidal venous drainage bed of the heart is still known as the thebesian system. His conception of the coronary arterial circulation, however, was erroneous in that he believed the aortic semilunar valves closed the openings of the coronary arteries during ventricular systole. In accordance with such a belief it is impossible for blood to enter the coronary arteries during the systolic phase of the cardiac cycle. He also wrote about "ossification" of the coronary arteries.

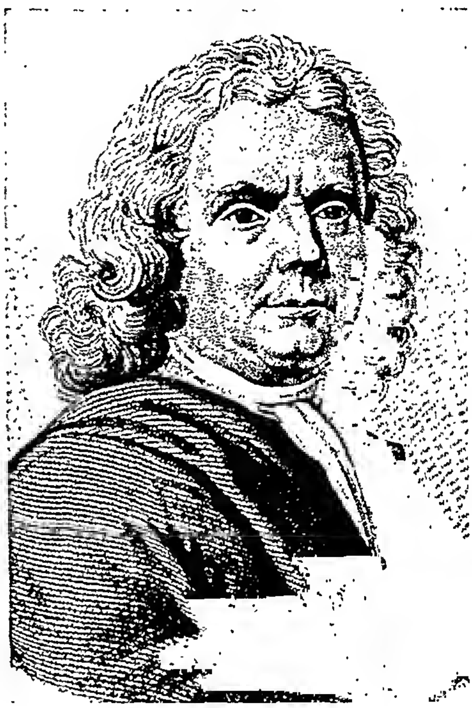
Pierre Dionis (?–1718), of Paris, was a distinguished surgeon, particularly noted for his cleverness in performing lithotomy and was surgeon to the Royal House of France. In 1690 he published a treatise on anatomy and in 1707 his famous work on surgery appeared, "Cours d'operations de chirurgie." Dionis was the founder of the Royal Academy of Surgery. But of greater interest to us is his publication, "Dissertation sur la mort subite avec l'histoire d'une fille cataleptique," Paris, L. d'Houry, 1710. In this publication Dionis reported two cases of painful disorder of the thorax which he ascribed to disease of the heart. These cases may well have been examples of the anginal syndrome of coronary disease.

The second record of treating aneurysm by the method of single ligation was that of Dominique Anel (1628–1725) of Toulouse. He was born the same year that William Harvey published his classic account of the

circulation of the blood. Anel's operation was performed in 1710, 116 years after Guillemeau's report (1594) and seventy-five years before John Hunter (1785) carried out the same procedure.

The first recorded instance of complete heart block was by a practicing physician of Laibach, Germany, Marcus Gerbezius (Verbez) (?–1718). He recorded many of his observations in the transactions of the Leopold Academy of Natural Sciences. Gerbezius observed and described two cases of extremely slow pulse associated with convulsive seizures. These observations certainly represented instances of complete heart block with convulsive syncope. Major translated this interesting account from the "Appendix ad epheridum Academiae Caesaro-Leopoldino-Carolinae Naturae Curiosum in Germania," Nuremberg, 1719, Centuriae VII et VIII, p. 23.

This reference appears to be the first one on heart block although Gerbezius was unaware of the nature of the condition or its relationship to the associated convulsive seizures. Gerbezius was also interested in the relationship of weather and climate to disease.



Hermann Boerhaave.

The master clinician and the leading systematist of the century was the Dutchman, Hermann Boerhaave (1668–1738), of Leyden. A great teacher who inspired his students, his lectures were attended by physicians from all parts of the continent and prominent patients traveled great distances to seek his advice and ministrations. Boerhaave was a Hippocratist in principle, a founder of the Eclectic School of Medicine and was an ardent advocate of the bedside method of medical instruction. Among his many illustrious pupils were von Haller and van Swieten.

In 1728 Boerhaave described the case of the Marquis de Saint Alban who died from suffocation resulting from a huge fatty mediastinal tumor and found the heart to be tremendously enlarged. He considered the foxglove (digitalis) a poison and therefore refused to prescribe it. He entertained a weird conception of the cause of fever, believing that it resulted from augmentation of cardiac activity meeting resistance in the capillary system.

Boerhaave taught and wrote not only on medicine but also on anat-

omy, pathology, chemistry and botany. Probably his most famous work was "Elementa chemiae," published at Leyden in 1732. "Institutiones medicae," published in 1708, was practically the first textbook on physiology. This, together with his "Aphorisms," was frequently reprinted and widely translated. Boerhaave's "Opera medica omnia" was published at Venice in 1766 and comprised treatises on chemistry, on methods of medical teaching, on syphilis, on diseases of the nervous system, and on the eye.

A clergyman and diversely gifted scientist, Stephen Hales (1677–1761) was born at Beckesbourne, Kent, and later lived at Teddington in Middlesex. He conducted a series of ingenious but rather crude experiments dealing with the hydrostatics of the circulation. Hales used horses, sheep and dogs in his experiments and attempted to measure blood pressure by inserting long glass tubes into an artery and recorded the height attained by the column of blood. He estimated the rate of the circulation and the velocity of the flow of blood in the veins and observed the constriction and dilatation of the capillaries. Hales also studied the behavior of the pulse by means of the sphygmoscope. He injected wax into the chambers of the heart and the aorta to obtain an idea of their capacity and these values were used in his computations. He estimated the blood pressure in man to be about 7½ feet (229 cm.) according to his system of measurement. These experiments were published in his book, "Statical essays: containing haemastatics, or, an account of some hydraulic and hydrostatical experiments made on the blood and blood-vessels of animals, also an account of some experiments on stones in the kidneys and bladder; with an inquiry into the nature of those anomalous concretions, to which is added, an appendix, containing observations and experiments relating to several subjects in the first volume, the greatest part of which were read at several meetings before the Royal Society," London, 1769. Hales's studies constituted the most important contributions relative to hemodynamics up to this time and it was not until much later that Jean-Marie Poiseuille (1799–1869) and

Stephen Hales.

Carl F. W. Ludwig (1816–1895) were to measure blood pressure by means of the mercury manometer.

Earlier, in 1727, Hales had published his work, "Vegetable staticks; or, an account of some statical experiments on the sap in vegetables." It is not improbable that these studies created the idea for Hales's subsequent studies on blood pressure.

He had been elected to the Royal Society of London in 1718.

In 1741 Hales, Sutton, a coffee-house keeper, and Martin Triewald, a captain of mechanics to the King of Sweden, had separately invented much-needed ventilators for the purpose of removing contaminated air from the lower decks of ships. An account of Triewald's invention was read before the Royal Society in 1742 and a year later Hales's work on ventilators appeared. It consisted of a large bellows which sucked out the foul air and could be operated either by hand or by a windmill. Soon ventilators were used in hospitals and prisons.

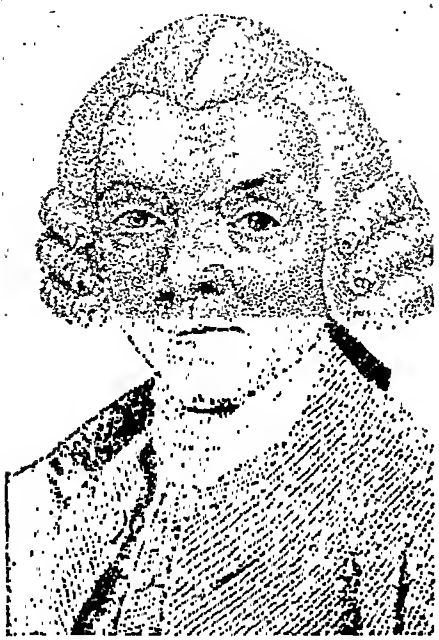
Jean-Baptiste de Sénac.

Another important contributor to the advancement of knowledge pertaining to the heart was one of France's most illustrious and versatile physicians, Jean-Baptiste de Sénac (1693–1770), of Versailles. He became chief physician to the Duke of Orleans in 1752 and treated the Dauphin while he was physician to Louis XV. De Sénac was a keen observer and meticulously recorded his findings. His famous work, "Traité de la structure du coeur, de son action et de ses maladies," published in two volumes, appeared first in 1749 and was so authoritative that medical authors late in the nineteenth century frequently referred to it.

De Sénac's contributions to cardiology were numerous and varied. He discussed asthma in relation to heart disease and called attention to orthopnea and edema of the legs, as manifestations of heart failure. He described the structure of the heart in detail and indicated the directions followed by the fibers of the myocardium. Observations were recorded indicating that the incidence of heart disease increased with age and he investigated the amount of epicardial fat present according to age periods. He made attempts to evaluate the degree of danger attending

wounds in various portions of the heart. De Sénac also made observations on instances of congenital cardiac defects and the significance of pericardial adhesions and commented on the use and abuse of blood-letting.

De Sénac also described cases of coronary sclerosis in which painful seizures did not occur, investigated the mode of production of cardiac dilatation, discussed the differentiation between pericardial and pleural effusion, advocated paracentesis for pericardial effusion and described an instance in which a murmur was so loud that it could be heard some distance from the patient. He noted and commented on atrophy of the heart. He further described marked thinning of the wall of the left ventricle (ventricular aneurysm) associated with coronary sclerosis.


William Hunter.

Earlier observers, as previously mentioned, had held the belief that the heart was immune to inflammation but de Sénac emphasized the fact that all structures of the heart were susceptible to inflammatory diseases.

An extremely interesting and important contribution of de Sénac was his comments on the use of quinine in what he termed "rebellious palpitations." It is not improbable that he was referring to the arrhythmia later to be known as auricular fibrillation and that the administration of quinine was actually the first application of the cinchona principle from which many years later the derivative, quinidine, was obtained. This report was contained in his "Traité de la structure du coeur," etc. under the translated caption, "Operation of stomachic remedies in palpitation, including the use of quinine in rebellious palpitations."

William Hunter (1718–1783), of Glasgow and London, a pupil of the famous English obstetrician Smellie, was primarily a surgeon and obstetrician. He was the older brother of the celebrated John Hunter and uncle of Matthew Baillie. His lectures on anatomy, surgery and gynecology were held in the famous anatomic theater and museum on Great Windmill Street and were extremely well attended. One of his prominent works, "The anatomy of the human gravid uterus," was published in 1774.

Hunter was the first to describe arteriovenous fistula. This description was recorded in "Medical observations and inquiries," London, 1762. Even as early as William Hunter's time the tendency to multiplicity of congenital cardiac defects had been noted. Hunter expressed the belief that pulmonary stenosis accounted for the multiple defects, not realizing that other defects, such as septal defects, not uncommonly occur without stenosis of the pulmonary artery or its orifice. The following brief citation from his work is adapted from Pettigrew's biographic review, and can be recognized as a description of the condition which later became known as the tetralogy of Fallot:

> 9. Three Cases of Mal-conformation of the Heart . . . The second case . . . the pulmonary artery was so small at its beginning, that it would barely give passage to a small probe; and the septum cordis was deficient, or perforated at the basis of the heart, so as to allow Dr. H.'s thumb (a small one), to pass across from one ventricle to the other, the orifice of the aorta being close to the perforation, so as to receive the blood from the right ventricle as well as from the left. This child lived thirteen years. The third case was of a still-born child at six months, the preparation of which was in Dr. H.'s museum. There was an opening of communication between the two ventricles, by which the blood of one cavity could pass into the other, without going through the usual circuit of the vessels.


Albrecht von Haller.

This appeared in 1784.

The greatest physiologist of this century was Albrecht von Haller (1708–1777) of Bern and Göttingen. A pupil of the celebrated Boerhaave, he dwarfed his master's accomplishments before his career was completed. With the founding of the University of Göttingen in 1736, Haller was appointed professor of anatomy, surgery and botany by King George II of England, who was also Elector of Hanover and Brunswick. Haller held these posts for seventeen years and during this time founded the Anatomical Museum and Laboratory, the Botanical School and Garden and the Department of Obstetrics and established a journal, "Göttinger Gelehrten Anzeiger," to which he contributed more than 12,000 book reviews. A prolific writer, he contributed some 13,000 scientific papers during his tenure at Göttingen. Among these were many dealing with the heart and circulation.

Haller described the musculature of the heart accurately and cor-

rectly and noted the changes that occurred during systole. He demonstrated the property of irritability of muscles and proved the automatism of the heart, thereby laying the groundwork for the myogenic theory of cardiac activity, which was not formulated until the following century. In observing the alternate distention and collapse of the jugular veins, Haller related these phenomena to the effect of gravity and the respiratory aspiration of the thorax.

Haller also described the structure of the pericardium and the valves of the veins correctly. He was the first to describe clearly calcification of the pericardium. This description appeared in his work, "Opuscula pathologica," Lausannae, 1755. It will be recalled that Baglivi had mentioned the condition in the preceding century.

In this work was also the demonstration of a fusiform aneurysm of the aorta. Haller also contributed to the science of embryology when he demonstrated that the heart of the chick embryo pulsated before any other structure manifested evidence of dynamic function.

In view of the fact that Haller was the first to give a detailed description of calcification of the pericardium, an unusual and interesting literary reference of nearly two centuries later is worthy of recollection. Hewitt in 1932 first reported this literary gem and in a publication during the same year, from which we quote, Smith and Willius cited the same account.

(Hewitt has called our attention to the story of "Ethan Brand" by Nathaniel Hawthorne (1804–1864), which contains a vivid description of the death of the main character who had a "heart of stone." The description is so vivid that one wonders if Hawthorne knew of a case. If not, it would be interesting to know the source of the tale. We feel that the story is so unique and so relevant that part of it is well worth quoting.)

"With his long pole in his hand, he (Bartram) ascended to the top of the kiln. After a moment's pause, he called to his son.

" 'Come up here, Joe!' he said.

"So little Joe ran up the hillock and stood by his father's side. The marble was all burnt into perfect snow-white lime. But on its surface, in the midst of the circle, snow-white too and thoroughly converted into lime, lay a human skeleton, in the attitude of a person, who after long toil, lies down to long repose. Within the ribs, strange to say, was the shape of a human heart.

" 'Was the fellow's heart made of marble?' cried Bartram, in some perplexity at this phenomenon.

" 'At any rate, it is burnt into what looks like special good lime, and taking all the bones together, my kiln is half a bushel the richer for him!'

"So saying, the rude lime-burner lifted his pole and, letting it fall upon the skeleton, the relics of Ethan Brand were crumbled into fragments."

While at Göttingen Haller collected the data for his huge and most authoritative work in physiology, "Elementa Physiologiae Corporis Humani," which was published at Lausanne in nine volumes between 1759 and 1769. Other contributions included a demonstration that the so-called salivary duct was a vein, a demonstration of the uterine musculature, a demonstration of the coni vasculosi of the epididymis, de-

scription of a number of hitherto unknown arteries, recognition of the higher situation of the urinary bladder above the pubes in children, description of the omentum and the demonstration of the tela cellulosa as a connective tissue substance.

His "Bibliothecae," comprising his bibliographies on anatomy, botany, surgery and medicine, included 52,000 works, indicative of his almost fabulous reading capacity.

The Earl of Clarendon (1609–1674), of London and Rouen, not a physician, gave one of the early descriptions of angina pectoris, published thirteen years before Heberden (1772) named the disorder. The Earl of Clarendon was an English statesman, writer and historian. In his memoirs, dealing with the year 1632 but not published until 1759, he recorded the manner of death of his father, who had suffered long from stone in the bladder. The following is a brief quotation from the account: ". . . and the pain in his arm seizing upon him, he fell down dead, without the least motion of any limb."

The Earl of Clarendon.

John Baptist Morgagni (1682–1771) (see special biography), of Bologna, Padua and Venice, was a pupil of Valsalva and Malpighi. He was the outstanding morbid anatomist of this era and was in reality the founder of systematic pathologic anatomy. His contributions to the field of cardiology are legion and the inclusion of all his important contributions would create a volume in itself. Morgagni's most celebrated work, "De sedibus et causis morborum per anatomen indagatis libri quinque," was published in 1761 and translated into English by Benjamin Alexander in 1769. This five volume work comprised seventy letters or communications. His descriptions of disease were remarkably accurate and he attempted to correlate pathologic findings with clinical phenomena, although at times these correlations were not entirely clear.

Morgagni described lesions of the aortic, mitral, pulmonary and tricuspid valves and presented instances of mitral stenosis, calcareous stenosis of the aortic valve and aortic regurgitation. He demonstrated coronary sclerosis and aneurysm of the aorta and described heart block. Like Fernel and Paré he believed that syphilis favored the de-

velopment of aneurysm but further stated that syphilis could produce changes in other arteries. Morgagni related dysphagia as an occasional symptom of both aneurysm and fibrinous pericarditis.

In observing changes in the myocardium, Morgagni ascribed the fibrous alterations to degenerative processes rather than to inflammation, a concept that was prevalent not only then but also in the twentieth century. He called attention to the patchy character of the fibrous regions and commented on their frequent location near the apex of the left ventricle and the lower portion of the interventricular septum. Rupture of the heart in instances of marked fatty myocardial changes was recorded. This in all probability represented cardiac infarction.

Morgagni described congenital cardiac defects and lesions of the endocardium and recognized and described pericardial effusion, adhesions and calcification. He believed that cyanosis resulted from venous stasis while many of his contemporaries were of the opinion that it resulted from the intermingling of arterial and venous blood. In studying the pulsations of the jugular veins he ascribed one impulse to contraction of the auricle and the other to contraction of the ventricle.

After a most productive life Morgagni died in his ninetieth year from spontaneous rupture of the heart, a condition which he had so accurately described during his tremendous postmortem experience.

One of the most important contributions of the eighteenth century was the discovery of percussion by Joseph Leopold Auenbrugger (1722–1809) (see special biography), of Vienna. He was a student of van Swieten and was connected with the Spanish Hospital at Vienna from 1751 to 1762, first as assistant and later as physician. A simple man of genius, he undoubtedly utilized certain facts that he had acquired during his childhood in the development of his discovery. During his time and probably earlier the method of tapping objects, such as barrels, to ascertain the fluid level of their contents was widely utilized.

Auenbrugger was the son of an Austrian innkeeper and working with his father had learned the method of tapping. He was also a musician, a fact which implies that he was endowed with a fine sense of perception of sound. Both these facts may have prompted him to study changes in resonance as determined by tapping various portions of the human body, especially the thorax.

For many years Auenbrugger worked with percussion and in 1761 his classic work appeared, "Inventum novum ex percussione thoracis humani, ut signo abstrusos interni pectoris morbos detegendi," Vienna. However, Gee asserted that a primitive form of percussion had been employed by the early Greeks before the time of Celsus (early part of the first century) in differentiating ascites from tympanites.

For nearly fifty years after Auenbrugger's exposition of his method, the profession refused to accept it and it was only after Corvisart's

translation of Auenbrugger's work in 1808 and his advocacy of percussion that the method became an integral part of physical diagnosis. Auenbrugger demonstrated, among many things, diseases of the lungs, empyema, pleural and pericardial effusions, extravasations of blood in the pleural and pericardial cavities and enlargement of the heart.

Frank Nicholls, an English physician, in 1761 reported the postmortem findings in the case of George II, who twenty-four years before his death had appointed von Haller to the chair of anatomy, surgery and botany at the new University of Göttingen. George II, the second of England's Hanover kings, had died in 1760 at the age of seventy-seven years. The king's death had occurred suddenly and at postmortem examination rupture of the right ventricle and a rent in the aorta were found. Burchell and Keys discussed this interesting report in a recent publication and raised the question whether death could justifiably be ascribed to coronary atheroma, occlusion, myocardial infarction and ultimate cardiac rupture. They commented on the rarity of rupture of the right ventricle and, in view of the accompanying rent in the aorta, considered the possibility that the entire pathologic process may have been a dissecting aneurysm of the aorta.

William Heberden.

Another interesting case of sudden death was reported by Nicholas François Rougnon de Magny, a French physician. In this instance severe thoracic pain terminated in sudden death of the patient. This description was contained in his "Lettre à Lorry" (1768). De Magny attributed the pain chiefly to ossification of the costal cartilages but also implied that it might result from fatty degeneration of the heart muscle fibers, accumulation of fat around the heart or the accumulation of blood in the chambers of the heart. According to Garrison, Hans Kohn did not believe that this case represented an instance of the anginal syndrome but rather one of pulmonary emphysema with dyspnea and cardiac dilatation.

One of the outstanding classic descriptions of all times was recorded by William Heberden (1710–1801), of London, a practicing physician endowed with keen powers of observation. He was a fellow of the Royal College of Physicians; this honor was bestowed on him in 1746. Heber-

den's famous work, "Commentaries on the history and cure of diseases," was published posthumously by his son, William, in 1802. However, much of the material had been written by Heberden as early as 1782. In this work Heberden recorded, described and named the clinical syndrome which has since that time been known as "angina pectoris" or as he expressed it, "pectoris dolor" (1772). Heberden's classic description of the anginal syndrome should be read by every physician because even today little could be added to, or subtracted from, its context.

> . . . But there is a disorder of the breast marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare, which deserves to be mentioned more at length. The seat of it, and sense of strangling, and anxiety with which it is attended, may make it not improperly be called angina pectoris.
>
> They who are afflicted with it, are seized while they are walking (more especially if it be up hill, and soon after eating), with a painful and most disagreeable sensation in the breast, which seems as if it would extinguish life, if it were to increase or to continue; but the moment they stand still, all this uneasiness vanishes.
>
> In all other respects, the patients are, at the beginning of this disorder, perfectly well, and in particular have no shortness of breath, from which it is totally different. The pain is sometimes situated in the upper part, sometimes in the middle, sometimes at the bottom of the os sterni, and often more inclined to the left than to the right side. It likewise very frequently extends from the breast to the middle of the left arm. The pulse is, at least sometimes, not disturbed by this pain, as I have had opportunities of observing by feeling the pulse during the paroxysm. Males are most liable to this disease, especially such as have past their fiftieth year.
>
> After it has continued a year or more, it will not cease so instantaneously upon standing still; and it will come on not only when the persons are walking, but when they are lying down, especially if they lie on the left side, and oblige them to rise up out of their beds. In some inveterate cases it has been brought on by the motion of a horse, or a carriage, and even by swallowing, coughing, going to stool, or speaking, or any disturbance of mind.
>
> Such is the most usual appearance of this disease; but some varieties may be met with. Some have been seized while they were standing still, or sitting, also upon first waking out of sleep; and the pain sometimes reaches to the right arm, as well as to the left, and even down to the hands, but this is uncommon: in a very few instances the arm has at the same time been numbed and swelled. In one or two persons, the pain has lasted some hours, or even days; but this has happened when the complaint has been of long standing, and thoroughly rooted in the constitution: once only the very first attack continued the whole night.

While Heberden had no clear concept regarding the true meaning of the syndrome, he, nevertheless, associated it with the heart and intimated that the pain was due to spasm of the heart itself. Heberden stated that he had observed about 100 such cases.

In the same year that Heberden wrote his classic description he received an anonymous letter, dated April 16, in which the writer of the letter gave a vivid account of his own sensations which "seem to indicate a sudden death." The anonymous writer further stated that there was "an universal pause within me of the operations of nature for perhaps three or four seconds."

Another important investigator of this century was Lazaro Spallanzani (1729–1799) of Scandiano. He was an outstanding physiologist and a pioneer in the field of experimental morphology. Spallanzani was professor of logic and metaphysics at both Reggio and Modena and later became professor of natural history and director of the Museum at Pavia. His investigations were varied and included studies of the cardiovascular and respiratory systems, digestion and generation.

Spallanzani investigated the role of the heart and circulation from the embryo to the adult. He was the first to show that the impetus given to the blood by the contraction of the heart was maintained throughout the entire arterial system as far as the smallest capillary. Spallanzani studied the capillary circulation, observed the circulation through the lungs and noted the velocity of the blood and the arterial dilatation produced by systole of the ventricle. He further observed that a heart chamber emptied itself during systole. Extensive observations, made of the circulation in embryos, appeared in his work "Dei fenomeni della circolazione osservata nel giro universale" (1777). His investigations also included the respiratory gaseous exchange in warm-blooded and cold-blooded animals.

Lazaro Spallanzani.

One of England's most wealthy and philanthropic physicians of this time was John Fothergill (1712–1780) of Edinburgh and London. He is said to have remarked after attaining affluence, "I climbed on the backs of the poor to the pockets of the rich." Fothergill was a graduate of Edinburgh and the son of a Quaker family that had suffered innumerable hardships and indignities in defense of their faith. He was a close friend of William Heberden and thus had learned about angina pectoris. Fothergill was also a personal friend of Benjamin Franklin, was sympathetic to the cause of the American colonies and exerted his influence in attempting to heal the breach between the colonies and the Mother Country.

In 1776 in his paper, "Further account of the angina pectoris," Fothergill presented the case of H. R., Esq., who died suddenly in a fit of anger. In describing the postmortem findings (the postmortem was performed

by John Hunter) he stated that the coronary arteries from their origin had "become one piece of bone." No comments were made, however, relating to the symptoms although Fothergill implied that the patient believed that he was afflicted with the disease described by Heberden. He was aware of the relationship of flatulence to the precipitation of the anginal seizures and advocated essence of peppermint to facilitate eructation of gas and mild laxatives to prevent constipation.

Fothergill was of the opinion that great and sustained muscular effort resulted in hypertrophy of the heart and advised against the administration of digitalis in disease of the aortic valve.


John Fothergill.

One of France's most distinguished chemists, Antoine-Laurent Lavoisier (1743–1794), deserves mention in the historical development of knowledge pertaining to the heart and the circulation. While chiefly interested in the physiology of respiration, which in essence is an integral part of circulatory physiology, his investigations placed the whole subject on a correct basis. Lavoisier demonstrated that respiration caused chemical alterations in the inspired air, that some of the air which entered the lungs did not come out as such and that some of the oxygen, or "vital air" as he called it, was absorbed by the blood. He disclosed that the stale air in close places could be quickly revitalized by oxygen. Many historians credit Lavoisier as being the true discoverer of oxygen.

The first description of the combination of congenital defects now known as the tetralogy of Fallot was recorded by Eduard Sandifort (1742–1814), the eminent Dutch anatomist, linguist and teacher. His description was classic and appeared in his "Observationes anatomico-pathologicae" in 1777.

The eighteenth century witnessed one of the most important therapeutic contributions of all times with reference to heart disease. It was William Withering (1741–1799) (see special biography), of Stafford and Birmingham, who introduced the foxglove (digitalis) in the treatment of the failing heart. His little book on the subject remains today as one of the medical classics. In addition to being a popular and suc-

cessful practitioner of medicine, he became a botanist of note and while practicing in Stafford published a comprehensive work, "A botanical arrangement of all the vegetables naturally growing in Great Britain," London, 1776.

After many years of clinical experimentation with foxglove, Withering finally published his conclusions. In the preface of his little volume, "An account of the foxglove," London, 1785, he wrote, "After being frequently urged to write upon this subject, and as often declining to do it, from apprehension of my own inability, I am at length compelled to take up the pen, however unqualified I may still feel myself for the task." It is variously recorded, whether it be legend or fact, that Withering had learned of the value of foxglove for the relief of dropsy from Old Mother Hutton, of Shropshire, who had successfully used a decoction of various herbs. Analyzing the formula, he soon discovered that the active ingredient was foxglove.

Antoine-Laurent Lavoisier.

Withering did not discover the drug digitalis but rather gave a clear and concise dissertation on its indications, methods of administration, effects, dosage and dangers. He was not certain as to its exact action but believed that it directly influenced the heart. Foxglove was known to some of the herbalists of the sixteenth and seventeenth centuries and was mentioned in early English and German herbals.

Withering's treatise is so clearly and wisely written that many of its passages could well be utilized as a modern text. It is another medical classic that every physician should read and remember.

John Hunter (1728–1793), of London, was the younger brother of the celebrated William Hunter. Both brothers contributed generously to English medicine. John Hunter was a well-trained anatomist and comparative anatomist before entering the field of surgery. He performed many postmortem examinations and stressed the importance of correlating clinical phenomena with the findings after death. Hunter investigated venereal disease extensively and held the erroneous opinion that syphilis and gonorrhea were one and the same disease. He carried his experiments to the point where he wittingly inoculated himself with

the discharge from syphilitic lesions and believed that he observed manifestations of both diseases.

In 1785 Hunter devised and performed his famous operation for aneurysm, which consisted in ligation of the artery at a point beyond the dilatation. However, Jacques Guillemeau (1550–1613) had performed single ligation for aneurysm in 1594.

Hunter also made observations pertaining to the cardiac valves and believed that the valves of the right side of the heart were not constructed as perfectly as those of the left chambers. This belief was gained by injecting fluids into the pulmonary artery, which resulted in regurgitation of fluid through both valvular barriers.


John Hunter.

Hunter's most outstanding works comprised the "Natural history of the human teeth," 1771; "On venereal disease," 1786; the "Observations on certain parts of the animal oeconomy," 1786; and the "Treatise on the blood, inflammation and gunshot wounds," 1794, the latter being published posthumously.

Hunter developed angina pectoris eight years prior to his death and once made the famous remark that his "life was in the hands of any rascal who chose to annoy and tease him." His prophecy was fulfilled when he became emotionally disturbed during a dispute with a colleague at St. George's Hospital.

Hunter's brother-in-law, Everard Home, published an account of the illness (1794) together with the postmortem findings, which disclosed marked coronary atheroma.

Robert Hamilton (1721–1793), of England, a practicing physician, was probably the first to refer to the hereditary factors of angina pectoris although Lancisi had called attention to hereditary influences pertaining to heart disease in general.

An important contributor during the closing years of this century was Matthew Baillie (1761–1823), of London. A nephew of the illustrious Hunter brothers on his maternal side and a student of his uncle, William Hunter, he became a prominent physician and lecturer. He was physician extraordinary to George III. Baillie succeeded William Hunter as lecturer in anatomy at the Great Windmill Street School in

association with the irascible William Cumberland Cruikshank (1754–1800) and held this post for fifteen years. In 1787 he was appointed physician to St. George's Hospital and was elected to fellowship in the Royal College of Physicians, London, in 1790.

Baillie's most celebrated work, "The morbid anatomy of some of the most important parts of the human body," was published in London in 1793. In 1788, first in the form of a letter to John Hunter and later under the title of "A remarkable transposition of the viscera" in the Philosophic Transactions of the Royal Society, Baillie described a case of congenital dextrocardia with complete situs inversus viscerum. He observed and described transposition of the great arterial trunks in which the aorta issued from the right ventricle and the pulmonary artery from the left ventricle. He also showed that death presumably resulting from the so-called cardiac polyp was in reality associated with intracardiac thrombi. Baillie further demonstrated that palpable pulsations of the abdominal aorta were not indicative of disease and he mentioned rheumatism of the heart, which had been discussed earlier by Pitcairn (1788).

Matthew Baillie.

Another important contribution of Baillie's was his article, "An account of a particular change of structure in the human ovarium." Baillie also described pulmonary emphysema in the case of Dr. Samuel Johnson.

Probably the first to associate rheumatism with disease of the heart was David Pitcairn (1711–1791), a prominent London physician and close personal friend of the brothers Hunter. He attended John Hunter on several occasions before Hunter's death. Pitcairn discussed "rheumatism of the heart" in 1788 but unfortunately this work was never published.

An early account of complete heart block was that of Thomas Spens (1769–1842), of Edinburgh. He was a practicing physician who was elected to fellowship in the Royal College of Physicians when he was only twenty-five years of age and during his membership in the college held the posts of librarian, president and treasurer. Spens reported the case of a fifty-four year old man who suffered from convulsive syncope and remarkable slowness of the pulse (twenty-four beats each

minute). After several episodes of unconsciousness, death suddenly occurred. Postmortem examination by gross inspection revealed no evident heart changes but Spens found that the ventricles of the brain contained about 2 ounces of fluid. He speculated on the cause of the patient's symptoms and death and postulated the possibility that hydrocephalus was responsible for the syndrome.

This communication was reported by Spens's friend, Dr. Duncan, in "Medical Commentaries," Edinburgh, in 1793. Only two previous reports of heart block had been published, the first by Gerbezius in 1719 and the other by Morgagni in 1761.

David Pitcairn.

A prominent surgeon of this era, John Abernethy (1764–1831), of London, conducted some interesting and important experiments on the heart in addition to performing certain daring surgical procedures on peripheral arteries. He was a student of John Hunter and later became his successor. In his lectures Abernethy eloquently defended his master's physiologic beliefs. He was the first to ligate the external iliac artery for aneurysm (1796) and in 1809 reported in his "Surgical observations," London, the four cases in which the procedure was employed, twice with success. In 1798 Abernethy ligated the common carotid artery for hemorrhage.

Near the close of the century Abernethy confirmed the experiments of Vieussens and Thebesius in his work, "Observations on the foramina thebesii of the heart," which appeared in the Philosophical Transactions of the Royal Society, London, in 1798. By making a "common coarse waxen injection" into the coronary arteries he observed that the wax flowed readily into the chambers of the heart. In 1793 he described an anomaly of the abdominal viscera which resembled the Eck fistula.

The man known throughout a grateful world for his monumental contribution in his discovery of vaccination against smallpox also contributed to the knowledge of heart disease. Edward Jenner (1749–1823), of Berkeley, Gloucestershire, was a kindly man who became a successful practitioner. The names and achievements of John Hunter, Edward Jenner and Caleb Hillier Parry, all celebrated English physi-

cians, are closely knit because they were contemporaries, close personal friends and all, by their free interchange of ideas, contributed to the advancement of knowledge pertaining to angina pectoris and coronary sclerosis.

By careful observation at the bedside and at the postmortem table, Jenner related angina pectoris with obliterative arteriosclerosis of the coronary arteries (1799). Ten years earlier (1789) Jenner had addressed the Fleece Medical Society on "Remarks on a disease of the heart following acute rheumatism." This manuscript was never published and subsequently became lost. It is historically known as the "Lost Manuscript." In addition to his medical talents Jenner was a bird fancier, played the violin and flute, wrote poetry and was interested in botany.

John Abernethy.

The final member of the famous triumvirate, Caleb Hillier Parry (1755–1822), of Bath, was a distinguished practitioner and an astute observer. He was a classmate and lifelong friend of Edward Jenner. In 1788 he became a licentiate of the Royal College of Physicians in London. Among his patients were the celebrated German astronomer and philosopher, William Herschel, Senior, and Admiral Lord George Rodney. Parry's son, William Edward, was the famous Arctic explorer who eventually became a Rear Admiral in the Royal British Navy. Parry was aware of the relationship of angina pectoris and diseases of the coronary arteries and recorded his observations in his volume, "An inquiry into the symptoms and causes of the syncope anginosa, commonly called angina pectoris; illustrated by dissections," 1799.

In 1789 he presented a paper before the Medical Society of London which was not published until 1792. Its title was "On the effects of compression of the arteries in various diseases, and particularly those of the head, with hints toward a new mode of treating nervous disorders." By compressing the carotid artery and thus diminishing the blood flow to the brain, Parry believed that he benefited patients who had fits. Also by applying a tourniquet to the arteries of the limbs he stated that he observed improvement when certain diseases of the extremities existed.

The first volume of Parry's "Elements of pathology and therapeutics" appeared in 1815 and his son, Charles Henry, republished the work and completed the second volume in 1825, three years after his father's death. In 1816 Parry published his work, "An experimental inquiry into the nature, cause and varieties of the arterial pulse." While some of his conclusions were erroneous, he, nevertheless, concluded correctly that the pulse wave is caused by the impulse given to the blood by the systole of the left ventricle.

Parry is also well known for his observations on exophthalmic goiter and the accompanying circulatory phenomena. These interesting conclusions were published under the title, "Enlargement of the thyroid gland in connection with enlargement or palpitation of the heart," and appeared in his "Collected works," London, 1:478–480, 1825.

Edward Jenner.

Caleb Hillier Parry.

SUMMARY

In deliberating the general tenor of the eighteenth century with special reference to the accumulation of knowledge relating to the heart and circulation, one is inclined to disagree with Garrison in his contention that the era was essentially one of retrogression. While a certain static influence prevailed through most of the century, nevertheless, a distinct change in medical thought and philosophy was being evolved, which proved to be an important steppingstone for subsequent medical events.

One very important evolution of the eighteenth century occurred in medical teaching. While earlier physicians had in a small measure undertaken bedside medical teaching and demonstration, the didactic form of lectureship prevailed quite universally. Bedside teaching and the ever-increasing interest in undertaking the correlation of symptoms and signs with postmortem revelations did much to place medical education on a much higher level. Men such as Vieussens, Morgagni, Baillie and others contributed generously in establishing morbid anatomy (pathology) as one of the major medical sciences and to doctrinate the desire ever to seek the truth.

Physiology matured considerably during this century. While methods of experimentation were still crude, it was a hopeful sign that the attempts at scientific inquiry superseded the speculation on function, which had so miserably dominated the previous eras. Stalwarts such as von Haller, Hales, Lavoisier and others dared the mysteries of the unknown to discover at least the partial truths in their respective investigations.

Through the ingenuity and patience of such investigators as Malpighi and van Leeuwenhoek in the previous century, Spallanzani and others, microscopy became an established science even in spite of the limitation of the early magnifying devices.

Great clinicians increased in number and gradually diseases of the heart became more clarified. Diseases hitherto not noticed or understood became described and named. The method of mediate percussion was discovered and utilized to some extent, adding the third factor in the still limited field of physical diagnosis. Heberden's classic description of angina pectoris was one of the clinical high lights of the century, as well as Withering's sagacious exposition of the use of digitalis.

REFERENCES

Baglivi

Castiglioni, Arturo: A history of medicine. (Translated by E. B. Krumbhaar.) New York, Alfred A. Knopf, 1941, pp. 539, 548 and 568.

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, pp. 258–259.

Guthrie, Douglas: A history of medicine. Philadelphia, J. B. Lippincott Company, 1946, p. 198.

Herrick, J. B.: A short history of cardiology. Springfield, Illinois, Charles C Thomas, 1942, p. 33.

Major, R. H.: Classic descriptions of disease; with biographical sketches of the authors. Ed. 2. Springfield, Illinois, Charles C Thomas, 1939, pp. 515–516.

Stenn, Frederick: Giorgio Baglivi. Ann. M. Hist. s. 3, 3:183–194 (May) 1941.

Albertini

Herrick, J. B.: Op. cit., pp. 46–47.

Vierordt, Hermann: Geschichte der Herzkrankheiten. In Puschmann, Theodor: Handbuch der Geschichte der Medizin. Jena, Gustav Fischer, 1903, vol. 2, pp. 635–637.

Drelincourt

Benson, R. L.: General review: The present status of coronary arterial disease. Arch. Path. & Lab. Med. 2:876–916 (Dec.) 1926.
Herrick, J. B.: Op. cit., pp. 37 and 209.
Willius, F. A.: Cardiac clinics. CXIV. The historic development of knowledge relating to the coronary circulation and its diseases: the eighteenth century. Proc. Staff Meet., Mayo Clin. 20:327 (Sept. 5) 1945.

Cowper

Archaeologica medica. XLI.—William Cowper, the anatomist. Brit. M. J. 1:160–161 (Jan. 15) 1898.
Beekman, Fenwick: Bidloo and Cowper, anatomists. Ann. M. Hist. 7:113–129 (Mar.) 1935.
*Cowper, William: Of ossifications or petrifactions in the coats of arteries, particularly in the valves of the great artery. Phil. Tr. Roy. Soc., London. 5 (abridged): 215–219, 1809.
Garrison, F. H.: Op. cit., p. 420.
Herrick, J. B.: Op. cit., p. 124.
McIntosh, W. A.: Cowper—the anatomist. Canad. M. A. J. 10:938–945 (Oct.) 1920.
Major, R. H.: Op. cit., pp. 368–374.
White, P. D.: Heart disease. Ed. 3, New York, The Macmillan Company, 1944, p. 956.
Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors. St. Louis, The C. V. Mosby Company, 1941, pp. 105–114.

Vieussens

Castiglioni, Arturo: Op. cit., p. 533.
Garrison, F. H.: Op. cit., p. 250.
Gibson, G. A.: Diseases of the heart and aorta. New York, The Macmillan Company, 1898, pp. 229, 313, 357, 436, 494 and 694.
Herrick, J. B.: Op. cit., pp. 42–43.
Major, R. H.: Op. cit., pp. 374–377.
Vierordt, Hermann: Op. cit., pp. 634–635.
Wearn, J. T., Mettier, S. R., Klumpp, T. G. and Zschiesche, Louise J.: The nature of the vascular communications between the coronary arteries and the chambers of the heart. Am. Heart J. 9:143–164 (Dec.) 1933.
White, P. D.: Op. cit., p. 614.
Willius, F. A.: Op. cit., p. 327.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 184–185 and 373.

Lancisi

Arcieri, J. P.: The circulation of the blood and Andrea Cesalpino of Arezzo. New York, S. F. Vanni, 1945, pp. 112–113 and 121.
Castiglioni, Arturo: Op. cit., pp. 562–563.
Garrison, F. H.: Op. cit., pp. 221 and 367.
Gibson, G. A.: Op. cit., pp. 357, 443 and 828.
Herrick, J. B.: Op. cit., pp. 44–47, 49–50, 143, 189, 191, 200, 209 and 217.
Major, R. H.: Op. cit., pp. 492–494.
Vierordt, Hermann: Op. cit., p. 635.
Wearn, J. T., Mettier, S. R., Klumpp, T. G. and Zschiesche, Louise J.: Op. cit., p. 144.
Willius, F. A.: Op. cit., pp. 327–328.
Willius, F. A. and Keys, T. E.: Op. cit., p. 174.

Floyer

Garrison, F. H.: Op. cit., pp. 355, 356 and 370.
Guthrie, Douglas: Op. cit., pp. 197 and 257.
Singer, Charles: A short history of medicine; introducing medical principles to students and non-medical readers. New York, Oxford University Press, 1928, p. 159.

Hoffmann

Castiglioni, Arturo: Op. cit., pp. 542, 584–585, 647 and 662.
Garrison, F. H.: Op. cit., pp. 314 and 392.
Gibson, G. A.: Op. cit., p. 757.
Willius, F. A.: Op. cit., p. 328.

Thebesius

Benson, R. L.: Op. cit., p. 876.
Gibson, G. A.: Op. cit., p. 67.
Herrick, J. B.: Op. cit., p. 209.
Wearn, J. T., Mettier, S. R., Klumpp, T. G. and Zschiesche, Louise J.: Op. cit., p. 144.
Willius, F. A.: Op. cit., p. 328.

Dionis

Castiglioni, Arturo: Op. cit., p. 553.
Garrison, F. H.: Op. cit., p. 341.
Guthrie, Douglas: Op. cit., p. 209.
Willius, F. A.: Op. cit., p. 328.

Anel

Garrison, F. H.: Op. cit., pp. 341 and 342.
Matas, Rudolph: Personal experiences in vascular surgery; a statistical synopsis. Ann. Surg. 112:802–839 (Nov.) 1940.

Gerbezius

Major, R. H.: Op. cit., pp. 352–353.

Boerhaave

Castiglioni, Arturo: Op. cit., pp. 615–617.
Garrison, F. H.: Op. cit., pp. 315–317.
Guthrie, Douglas: Op. cit., pp. 60, 80, 190, 203, 216, 217, 220, 221, 227, 228, 230 and 231.
Herrick, J. B.: Op. cit., pp. 39–40.
Singer, Charles: Op. cit., pp. 140–142.
Vierordt, Hermann: Op. cit., p. 636.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 167, 191 and 234.

Hales

Archaeologica medica. XXXVI.—Stephen Hales, a pioneer in modern physiology. Brit. M. J. 2:1191 (Oct. 23) 1897.
Burget, G. E.: Stephen Hales (1677–1761). Ann. M. Hist. 7:109–116 (June) 1925.
Castiglioni, Arturo: Op. cit., p. 614.
Dawson, P. M.: The biography of Stephen Hales, D.D., F.R.S. Bull. Johns Hopkins Hosp. 15:185–192 (June) 1904.

Dawson, P. M.: Stephen Hales, the physiologist. Bull. Johns Hopkins Hosp. 15: 232–237 (July-Aug.) 1904.
Garrison, F. H.: Op. cit., p. 322.
Guthrie, Douglas: Op. cit., pp. 260–261.
°Hales, Stephen: An account of some hydraulic and hydrostatical experiments made on the blood and blood-vessels of animals, etc. Ed. 3, London, Wilson & Nicol, 1769, vol. 2, 354 pp.
Herrick, J. B.: Op. cit., p. 39.
Major, R. H.: The history of taking the blood pressure. Ann. M. Hist. n.s. 2:47–55 (Jan.) 1930.
White, P. D.: Op. cit., p. 92.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 125–155.

de Sénac

Castiglioni, Arturo: Op. cit., p. 624.
Degris, Georges: Étude sur Sénac, premier médecin de Louis XV (1693–1770). Paris, L. Boyer, 1901, 78 pp.
Garrison, F. H.: Op. cit., p. 370.
Gibson, G. A.: Op. cit., pp. 284, 313, 314, 644, 694 and 766.
Herrick, J. B.: Op. cit., pp. 49, 50 and 209.
Long, E. R.: A history of pathology. Baltimore, The Williams & Wilkins Company, 1928, 291 pp.
Renouard, P.-V.: History of medicine, from its origin to the nineteenth century, with an appendix, containing a philosophical and historical review of medicine to the present time. (Translated by C. G. Comegys.) Cincinnati, Ohio, Moore, Wilstach, Keys & Co., 1856, 719 pp.
°de Sénac, J. B.: Traité de la structure du coeur, de son action et de ses maladies. Paris, J. Vincent, 1749, vol. 2, p. 524.
Vierordt, Hermann: Op. cit., pp. 637–638.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 157–163.

William Hunter

Castiglioni, Arturo: Op. cit., p. 596.
Garrison, F. H.: Op. cit., p. 340.
Gibson, G. A.: Op. cit., p. 292.
Guthrie, Douglas: Op. cit., pp. 222, 229, 237, 238, 240 and 351.
Pettigrew, T. J.: Medical portrait gallery. Biographical memoirs of the most celebrated physicians, surgeons, etc., etc., who have contributed to the advancement of medical science. London, Fisher, Son & Co., 1840, vol. 2, pp. 3–4.

von Haller

Castiglioni, Arturo: Op. cit., pp. 609–611.
Fulton, J. F.: Annual oration of the Boston Medical Library; Haller and the humanization of bibliography. New England J. Med. 206:323–328 (Feb. 18) 1932.
Garrison, F. H.: Op. cit., pp. 317–319.
Gibson, G. A.: Op. cit., pp. 6, 60 and 198.
°Haller, Albertus: Opuscula pathologica, partim recusa partim inedita quibus sectiones cadaverum morbosorum potissimum continentur. Accedunt experimenta de respiratione, quarte parte aucta. Lausannae, Bousquet et soc., 1755, p. 135.
Hemmeter, J. C.: Albrecht von Haller: scientific, literary, and poetical activity. Bull. Johns Hopkins Hosp. 19:65–74 (Mar.) 1908.
Herrick, J. B.: Op. cit., p. 40.
Hewitt, R. M.: Correspondence; Nathaniel Hawthorne's report of a case of pericarditis calculosa. J. A. M. A. 98:68 (Jan. 2) 1932.
Major, R. H.: Op. cit. (Classic descriptions of disease), pp. 441–443.

Pettigrew, T. J.: Op. cit., vol. 1, 10 pp.
Singer, Charles: Op. cit., pp. 142–145.
Smith, H. L. and Willius, F. A.: Pericarditis; chronic adherent pericarditis. Arch. Int. Med. 50:171–183 (Aug.) 1932.
Smith, H. L. and Willius, F. A.: Pericarditis; calcification of pericardium. Arch. Int. Med. 50:184–191 (Aug.) 1932.
Smith, H. L. and Willius, F. A.: Pericarditis; pericarditis with effusion. Arch. Int. Med. 50:192–202 (Aug.) 1932.
Smith, H. L. and Willius, F. A.: Pericarditis; fibrinous pericarditis and "soldier's patches." Arch. Int. Med. 50:410–414 (Sept.) 1932.
Smith, H. L. and Willius, F. A.: Pericarditis; terminal pericarditis. Arch. Int. Med. 50:415–418 (Sept.) 1932.
Vierordt, Hermann: Op. cit., pp. 634 and 646.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 165–170.

Earl of Clarendon

Garrison, F. H.: Op. cit., pp. 272 and 359.
Hyde, Edward (Earl of Clarendon): The life of Edward, Earl of Clarendon, Lord High Chancellor of England and Chancellor of the University of Oxford. Oxford, 1857.
Major, R. H.: Op. cit. (Classic descriptions of disease), pp. 452–455.
Willius, F. A.: Op. cit., p. 329.
Willius, F. A. and Keys, T. E.: Op. cit., p. 219.

Morgagni

Adams, E. W.: Founders of modern medicine.—II. Giovanni Battista Morgagni. (A. D. 1682–1771). M. Library & Hist. J. 1:270–277 (Oct.) 1903.
Benson, R. L.: Op. cit., p. 876.
Castiglioni, Arturo: Op. cit., pp. 602–608.
Garrison, F. H.: Op. cit., pp. 353–354.
Gibson, G. A.: Op. cit., pp. 199, 228, 284, 328, 384, 390, 679, 682–683, 716, 753 and 843.
Guthrie, Douglas: Op. cit., pp. 245, 251 and 281.
Gross, Louis: The blood supply to the heart; in its anatomical and clinical aspects. New York, Paul B. Hoeber, 1921, p. 78.
Herrick, J. B.: Op. cit., p. 209.
Long, E. R.: Op. cit., pp. 44, 53, 56, 60, 99, 101, 109, 110–118, 123, 152 and 271.
Major, R. H.: Op. cit. (Classic descriptions of disease), pp. 354–358, 377–378, 402 and 494–499.
*Morgagni, J. B.: The seats and causes of diseases investigated by anatomy; in five books containing a great variety of dissections, with remarks. (Translated by Benjamin Alexander.) London, A. Millar, 1769, vols. 1, 2 and 3.
Nicholls, A. G.: Morgagni, the father of modern pathology: an appreciation and a comparison. Montreal M. J. 32:40–51, 1903.
Pettigrew, T. J.: Op. cit., vol. 1, 4 pp.
Singer, Charles: Op. cit., p. 157.
Vierordt, Hermann: Op. cit., pp. 630, 635–637, 642, 644 and 659.
White, P. D.: Op. cit., p. 957.
Willius, F. A.: Op. cit., pp. 329–330.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 171–187.

Auenbrugger

Castiglioni, Arturo: Op cit., pp. 618–619.
*Forbes, John: Texts and documents on percussion of the chest; being a translation of Auenbrugger's original treatise entitled "Inventum novum ex percussione thoracis humani, ut signo abstrusos interni pectoris morbos detegendi." [Vienna, 1761] Bull. Inst. Hist. Med. 4:379–403 (May) 1936.

Garrison, F. H.: Op. cit., pp. 352–353.
Gee, S. J.: Auscultation and percussion; together with the other methods of physical examination of the chest. Ed. 2, London, Smith, Elder & Co., 1877, p. 56.
Gibson, G. A.: Op. cit., pp. 135, 313 and 721.
Guthrie, Douglas: Op. cit., pp. 258, 259 and 366.
Herrick, J. B.: Op. cit., p. 76.
Major, R. H.: Op. cit. (Classic descriptions of disease), pp. 443–444 and 614–617.
Nova et vetera: Leopold Auenbrugger. The discovery of percussion. Brit. M. J. 1: 1191–1192 (May 15) 1909.
Otis, E. O.: Auenbrugger and Laennec, the discoverers of percussion and auscultation. Boston M. & S. J. 139:281–285 (Sept. 22); 305–308 (Sept. 29) 1898.
Singer, Charles: Op. cit., p. 160.
Vierordt, Hermann: Op. cit., pp. 638–639.
White, P. D.: Op. cit., p. 52.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 189–213.

Nicholls

Burchell, H. B. and Keys, T. E.: The heart of George II of England. Bull. M. Library A. 30:198–202 (Apr.) 1942.
Nicholls, Frank: Observations concerning the body of his late Majesty, October 26, 1760. Phil. Tr. Roy. Soc., London. 11(abridged):574–579, 1809.
Smollett, T.: Quoted by Burchell, H. B. and Keys, T. E.
Willius, F. A.: Op. cit., pp. 330–331.

Rougnon

Garrison, F. H.: Op. cit., p. 358.
Gibson, G. A.: Op. cit., pp. 758–760.
Herrick, J. B.: Op. cit., pp. 217–218.
Rougnon [de Magny], N. F.: Lettre à M. Lorry, touchant les causes de la mort de feu Monsieur Charles, ancien capitaine de cavalerie, arrivée à Besançon le 23 fevrier, 1768. Besançon, J.-F. Charmet, 1768, 55 pp.
Willius, F. A.: Op. cit., p. 331.

Heberden

Castiglioni, Arturo: Op. cit., p. 620.
Crummer, LeRoy: William Heberden's An introduction to the study of physic [now for the first time published]. New York, Paul B. Hoeber, Inc., 1929, 159 pp.
Davidson, P. B.: William Heberden, M.D., F.R.S. Ann. M. Hist. 4:336–346, 1922.
Garrison, F. H.: Op. cit., pp. 358–359.
Gibson, G. A.: Op. cit., pp. 248 and 760–762.
Guthrie, Douglas: Op. cit., pp. 69, 235 and 256.
°Heberden, William: Commentaries on the history and cure of diseases. London, S. Hamilton, 1802, 481 pp.
Herrick, J. B.: Op. cit., pp. 54–58 and 61.
Major, R. H.: Op. cit. (Classic descriptions of disease), pp. 455–459.
Pettigrew, T. J.: Op. cit., vol. 3, 18 pp.
Singer, Charles: Op. cit., p. 22.
Vierordt, Hermann: Op. cit., p. 621.
White, P. D.: Op. cit., pp. 816–818.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 215–224.

Spallanzani

Arcieri, J. P.: Op. cit., pp. 126–128.
Castiglioni, Arturo: Op. cit., pp. 612–613.
Garrison, F. H.: Op. cit., pp. 322–323.
Guthrie, Douglas: Op. cit., pp. 317–318.

Fothergill

*Fothergill, John: XXII. Farther account of the angina pectoris. Med. Obs. Soc. Phys., London, 5:233–258, 1776.
Garrison, F. H.: Op. cit., pp. 359–360.
Gibson, G. A.: Op. cit., pp. 505, 735, and 761.
Guthrie, Douglas: Op. cit., pp. 235, 238, 249–250, 251, 252, 253, 254 and 321.
Herrick, J. B.: Op. cit., pp. 58–59.
Major, R. H.: Op. cit. (Classic descriptions of disease), pp. 156–158 and 459–460.
Willius, F. A. and Keys, T. E.: Op. cit., p. 218.

Lavoisier

Castiglioni, Arturo: Op cit., p. 614.
Garrison, F. H.: Op. cit., pp. 329–330.
Singer, Charles: Op. cit., pp. 155–156.

Sandifort

Bennett, L. R.: Sandifort's "Observationes," Chapter I, concerning a very rare disease of the heart. Bull. Hist. Med. 20:539–570 (Nov.) 1946.

Withering

Castiglioni, Arturo: Op. cit., pp. 620–621.
Cushny, A. R.: William Withering, M.D., F.R.S. Proc. Roy. Soc. Med. (Section of the History of Medicine.) 8:85–93 (Mar. 17) 1915.
Garrison, F. H.: Op. cit., pp. 356–357.
Guthrie, Douglas: Op. cit., pp. 235, 256 and 257.
Herrick, J. B.: Op. cit., pp. 64 and 68.
Kolipinski, Louis: William Withering and his book on the foxglove. M. Record. 86:8–14 (July 4) 1914.
Major, R. H.: Op. cit. (Classic descriptions of disease), pp. 479–485.
Roddis, L. H.: William Withering; and the introduction of digitalis into medical practice. Ann. M. Hist. n.s. 8:93–112 (Mar.); 185–201 (May) 1936.
Shryock, R. H.: The development of modern medicine: an interpretation of the social and scientific factors involved. Philadelphia, University of Pennsylvania Press, 1936, pp. 1–2.
Singer, Charles: Op. cit., p. 328.
Vierordt, Hermann: Op. cit., p. 647.
White, P. D.: Op. cit., pp. 766–767.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 225–252.
*Withering, William: An account of the fox-glove, and some of its medical uses; with practical remarks on dropsy and other diseases. Birmingham, G. G. J. & J. Robinson, 1785, 207 pp.

John Hunter

Benson, R. L.: Op. cit., p. 877.
Castiglioni, Arturo: Op. cit., pp. 596–597.
Garrison, F. H.: Op. cit., p. 571.
Gibson, G. A.: Op. cit., pp. 570–571.
Guthrie, Douglas: Op. cit., pp. 121, 148, 164, 182, 235, 240–242, 243, 244, 247, 273, 277, 285, 329 and 338.
Herrick, J. B.: Op. cit., p. 210.
*Hunter, John: A treatise on the blood, inflammation, and gunshot wounds. To which is prefixed a short account of the author's life, by Everard Home. London, G. Nicoll, 1794, 575 pp.
Major, R. H.: Op. cit. (Classic descriptions of disease), pp. 48–51.
Ottley, Drewry: The life of John Hunter, F.R.S. In Palmer, J. F.: The works of

John Hunter, F.R.S.; with notes. London, Longman, Rees, Orme, Brown, Green, and Longman, 1835, vol. 1, pp. 1–198.
Parry, T. W.: Immortal names and other poems. London, The Mitre Press, 1937, 122 pp.
Singer, Charles: Op. cit., pp. 165–166.
Willius, F. A.: Op. cit., p. 334.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 263–275.

Hamilton

Allbutt, Clifford: Diseases of the arteries including angina pectoris. London, Macmillan and Co., Limited, 1915, vol. 2, p. 252.
*Hamilton, Robert: . . . from which it would appear that the complaint is sometimes hereditary. M. Commentaries, London. 9:307–316, 1785.
Willius, F. A.: Op. cit., p. 335.

Baillie

Bailey, J. B.: Heroes of medicine. Matthew Baillie. An autobiography, entitled "A short memoir of my life, with a view of furnishing authentic materials." Practitioner. 57:51–65 (July) 1896.
*Baillie, Matthew: Of a remarkable transposition of the viscera. Phil. Tr. Roy. Soc., London. 16(abridged):483–489, 1809.
Castiglioni, Arturo: Op. cit., p. 609.
Garrison, F. H.: Op. cit., pp. 354–355.
Gibson, G. A.: Op. cit., pp. 290–292, 390 and 397.
Guthrie, Douglas: Op. cit., pp. 235, 246, 254, 255, 277 and 281.
Herrick, J. B.: Op. cit., pp. 68–69.
Macmichael, William: The gold-headed cane. New York, Paul B. Hoeber, 1915, chap. 5, pp. 225–253.
Major, R. H.: Op. cit. (Classic descriptions of disease), pp. 637–639.
Pettigrew, T. J.: Op. cit., vol. 2, 10 pp.
Singer, Charles: Op. cit., p. 158.
Vierordt, Hermann: Op. cit., pp. 639 and 645.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 253–262.

Pitcairn

Gibson, G. A.: Op. cit., pp. 313 and 317.
Herrick, J. B.: Op. cit., p. 153.
Willius, F. A. and Keys, T. E.: Op. cit., p. 293.

Spens

Major, R. H.: Op. cit. (Classic descriptions of disease), p. 358.
*Spens, Thomas: I. History of a case in which there took place a remarkable slowness of the pulse. M. Commentaries (1792), Edinburgh. 7:458–465. 1793.
Willius, F. A. and Keys, T. E.: Op. cit., p. 396.

Abernethy

*Abernethy, John: Observations on the foramina thebesii of the heart. Phil. Tr. Roy. Soc., London. 18(abridged):287–290, 1809.
Castiglioni, Arturo: Op. cit., p. 598.
Garrison, F. H.: Op. cit., pp. 348–349.
Guthrie, Douglas: Op. cit., pp. 241, 242–243, 312 and 316.
Wearn, J. T., Mettier, S. R., Klumpp, T. G. and Zschiesche, Louise J.: Op. cit., pp. 143–164.
Willius, F. A.: Op. cit., p. 335.
Willius, F. A. and Keys, T. E.: Op. cit., p. 266.

Jenner

Garrison, F. H.: Op. cit., pp. 372–375.
Gibson, G. A.: Op. cit., p. 761.
Guthrie, Douglas: Op. cit., pp. 241, 247–249, 252, 257, 284 and 353.
Herrick, J. B.: Op. cit., pp. 210–211, 218 and 224.
Keil, Harry: A note on Edward Jenner's lost manuscript on "Rheumatism of the heart." Bull. Hist. Med. 7:409–411 (Apr.) 1939.
Major, R. H.: Op. cit. (Classic descriptions of disease), pp. 678–680.
Willius, F. A.: Op. cit., p. 334.
Willlus, F. A. and Keys, T. E.: Op. cit., pp. 217, 218, 266, 293, 385 and 817.

Parry

Benson, R. L.: Op. cit., p. 877.
Castiglioni, Arturo: Op. cit., p. 621.
Garrison, F. H.: Op. cit., p. 360.
Gross, Louis: Op. cit., p. 79.
Herrick, J. B.: Op. cit., pp. 210–211.
Major, R. H.: Op. cit. (Classic descriptions of disease), pp. 293–294.
*Parry, C. H.: An inquiry into the symptoms and causes of the syncope anginosa, commonly called angina pectoris. London, Cadell & Davis, 1799, 167 pp.
Willius, F. A.: Op. cit., pp. 334–335.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 385–386.

* Indicates original source consulted by the authors.

THE FIRST HALF OF THE NINETEENTH CENTURY

*The physician sees patients and not diseases.**

During the first half of the nineteenth century and even beyond, France was the medical mecca of the world. The closing years of the eighteenth century and the opening years of the nineteenth century witnessed the great social-democratic movement which followed the political revolutions both in France and America. The Napoleonic era, 1795 to 1815, represented a period in history in which most of Europe was in the throes of wars and changing power alliances and victorious aggression occurred, only to culminate in ultimate defeat. For many years, France remained literally untouched, for the wars were largely waged on foreign soil and the principle of the revolution was designed to free the people from the tyrannic bonds of royalty and to afford them opportunities for self-development.

Pierre-Joseph Desault.

Napoleon was a realist and possessed a breadth of vision which included the concept that scientific knowledge should be expanded and utilized for the betterment and the material needs of mankind. He encouraged the development of industry, recognized the potentialities of integrated sciences such as chemistry, physics and biology, and advocated the further development of the medical sciences, including the establishment of medical schools, hospitals, public health measures and so forth. The ascendancy of France brought forth not only military and political personalities of unusual ability, but also a line of great scientists and physicians. Napoleon emphasized the importance of human endeavor and is credited with the famous words, *"La carrière ouverte aux talens"* (The tools to those who can handle them).

* Paul-Louis Duroziez, Preface to "Traité clinique du coeur," 1891.

British medicine forged ahead in the second quarter of the century while German and Austrian medicine reached great heights of popularity in the last quarter. The nineteenth century, as far as medicine was concerned, was truly an era of progress.

A pioneer in the surgical treatment of aneurysm was the Frenchman, Pierre-Joseph Desault (1744–1795), who was the teacher of the celebrated anatomist, Marie-François-Xavier Bichat (1771–1802). Desault was professor of practical surgery and chief surgeon of the Hôtel Dieu. He was an advocate of the distal ligation of aneurysms. His work appeared posthumously in "Oeuvres chirurgicales," Paris, 1801.

Desault was the originator of the surgical journal, "Journal de Chirurgie," (1791–1792) and wrote extensively on the treatment of fractures.


Antonio Scarpa.

Anatomic discoveries and more accurate descriptions of previously discovered structures continued to be forthcoming in this century. Antonio Scarpa (1747–1832), of Venice, was a pupil of Morgagni, and in 1767, when only twenty years of age, was appointed professor of anatomy at Modena. His brilliant work and talents of organization led to his appointment as professor of anatomy at Pavia in 1783. During his twenty year tenure at Pavia, Scarpa was also made professor of clinical surgery and reconstructed and reorganized the Anatomical Institute. In addition to his anatomic skill, he was possessed of remarkable artistic talents which permitted him to illustrate his works with some of the most superb drawings.

In 1794, in his "Tabulae neurologicae," Pavia, he gave the most accurate description of the cardiac nerves yet to appear. Scarpa's work, "Sull' aneurisma principal: malattie degli occhi," appeared in 1801 and was a standard text of ophthalmology for many years. He was the first to regard arteriosclerosis as a lesion of the inner coats of the arteries (1804) and contended that the intima and media of arteries were ruptured in aneurysm.

Scarpa's "Anatomicae annotationes" was published in 1779. In 1789, he published his "Anatomicae disquisitiones de auditu et olfactu" which contained his discovery and description of the membranous labyrinth and the nasopalatine nerve. He also described the triangle in the thigh

which is still known by his name and the cremasteric fascia which is known as Scarpa's fascia.

Without a doubt, the most outstanding clinician since de Sénac, and the most brilliant of the first half of the nineteenth century, was Jean-Nicolas Corvisart (1755–1821), of Paris. He was professor of medicine at the Collège de France and personal physician to Napoleon Bonaparte. Many of Corvisart's contributions dealing with the heart and circulation appeared in his famous work, "Essai sur les maladies et les lésions organiques du coeur et des gros vaisseaux," Paris, 1806. Even at the close of the century, many medical authors referred to this book.


Jean-Nicolas Corvisart.

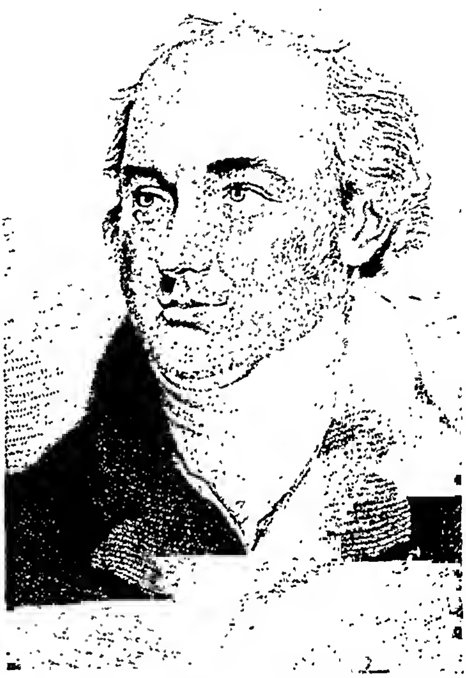
Corvisart distinguished between cardiac hypertrophy and dilatation and emphasized the point that an enlarged heart is a diseased heart. He showed that this was revealed both by clinical means and by postmortem examination. Corvisart was an ardent advocate of postmortem examination and in his teaching stressed the importance of proving the correctness or error of clinical diagnosis. He distinguished between organic and functional disturbances of the heart, separated heart failure into three stages and discussed the relationship of valvular lesions to the development of heart failure.

Corvisart was one of the first to mention and interpret palpable thrills over the precordium in the diagnosis of cardiac disease (*un bruissement particulier difficile à décrire*) and he particularly stressed the diagnostic importance of the thrill in mitral stenosis. He described fibrinous pericarditis, stating that the massive deposition of fibrin caused the pericardium to resemble the reticulum of the second stomach of the calf. Corvisart also recognized tubercles of the pericardium and recorded an instance of massive pericardial effusion in which 4 liters of fluid were present. He described the clinical symptoms and the postmortem findings in tricuspid stenosis and discussed myocarditis and its frequent association with endocarditis and pericarditis. Corvisart was thus one of the first to evolve the concept of pancarditis. He observed that an increased area of precordial pulsation occurred with cardiac dilatation and he was of the opinion that coronary sclerosis limited the development of cardiac hypertrophy.

Corvisart did not mention angina pectoris and only casually referred to disease of the coronary arteries. This appears to be an amazing omission, for contributions of the preceding century had established angina pectoris as a clinical entity. Herrick commented on this oversight, in his statement:

> To explain why this leading exponent of cardiology, whether one regards him as a practitioner, teacher or text book author in the medical center of the world, overlooked this subject, one must consider not only Corvisart's personality, but must in imagination retroject oneself to the beginning of the last century to see the conditions that prevailed. News traveled slowly in those days; medical journals and medical books might be greatly delayed in crossing the channel, for England and France were at war; national pride might have played a part in causing Paris physicians to ignore those of London.

In 1808, Corvisart, after many years of experience with percussion, translated Auenbrugger's work, added his own experience and gave Auenbrugger full credit as the discoverer of the method. The translation and commentary were published under the title, "Nouveau méthode pour reconnaître les maladies internales de la poitrine." The acclaim thus given to Auenbrugger's work by a widely known and popular clinician soon assured its universal acceptance.



Sir Astley Paston Cooper.

A pioneer in vascular surgery who gained an amazing experience in this field early in the nineteenth century was Sir Astley Paston Cooper (1768–1841), of Norfolk and London. He was a student of John Hunter and became one of the most distinguished surgeons of London. Cooper became demonstrator of anatomy at St. Thomas' Hospital when only twenty-one years of age and surgeon to Guy's Hospital in 1800.

He successfully ligated the common carotid and the external iliac arteries for aneurysm in 1808. Nine years later he performed the then unbelievable feat of ligation of the abdominal aorta. This operation was reported in his "Surgical essays," 1818, published in collaboration with Benjamin Travers (1783–1858).

Cooper's works included books on hernia, injuries of joints, diseases of the testicles and the anatomy of the thymus.

A young man, whose career was cut short by death in his thirty-second

year, made important contributions to the knowledge of the heart and circulation. Allan Burns (1781–1813), of Glasgow, is not well known in the annals of medical history, but deserves a wide acquaintanceship because of his advanced ideas. A lecturer in anatomy, assisting his elder brother, John, who was extramural lecturer on anatomy and surgery at Glasgow, Allan Burns never received his degree in medicine and was therefore unable to practice medicine but was permitted to assist his brother and his medical friends. In 1935, Herrick published an interesting commentary on the life and the works of Allan Burns.

Burns was an early exponent of the belief that angina pectoris occurs as the result of myocardial ischemia. While coronary sclerosis had been demonstrated on several previous occasions in cases of angina pectoris, the general concept prevailed that the symptoms resulted from a nervous affection of the heart. Burns conducted experiments in which he secured a moderately light ligature around a limb and found that under the stress of exercise the ligatured limb fatigued readily and became painful. These observations were so important and so universally ignored until nearly two decades of the twentieth century had passed that it seems important to quote from Burns's original work.

> In health, when we excite the muscular system to more energetic action than usual, we increase the circulation in every part, so that to support this increased action, the heart and every other part has its power augmented. If, however, we call into vigorous action, a limb, round which we have with a moderate degree of tightness applied a ligature, we find that then the member can only support its action for a very short time; for now its supply of energy and its expenditure do not balance each other: consequently, it soon, from a deficiency of nervous influence and arterial blood, fails and sinks into a state of quiescence. A heart, the coronary vessels of which are cartilagenous or ossified, is in nearly a similar condition; it can, like the limb, be girt with a moderately light ligature, discharge its functions so long as its action is moderate and equal. Increase, however, the action of the whole body, and along with the rest, that of the heart, and you will soon see exemplified, the truth of what has been said; with this difference, that as there is no interruption to the action of the cardial nerves, the heart will be able to hold out a little longer than the limb.

This and other observations were recorded in his book "Observations on some of the most frequent and important diseases of the heart; on aneurism of the thoracic aorta; on preternatural pulsation in the epigastric region; and on the unusual origin and distribution of some of the large arteries of the human body, illustrated by cases," Edinburgh, 1809.

The introductory paragraph to this work is of unusual interest and almost prophetic of modern concepts regarding the heart.

> The heart, from the intricacy of its structure, and from its incessant action, is liable to many diseases, and these from the importance of the function of this organ, are at all times highly alarming. Some of them are extremely insidious in their commencement, are attended with obscure and perplexing symptoms and in their result are almost uniformly and speedily fatal.

While not all of Burns's concepts regarding the heart and its diseases

were correct according to present-day standards, it is evident that his processes of thought were clear and logical and the reader must bear in mind the fact that his observations were made before the discovery of auscultation and other adjunct methods of diagnosis. Even though a young man, he had the courage of his convictions and openly and often sarcastically disagreed with his elders and predecessors. From the following quotation, it is possible that Burns had observed a thrombus in a coronary artery:

> In some, as in the case of Mr. Bellamy, dissected by Mr. Paytherus, their [the coronary arteries'] inner surface has been found crusted over with a lymphatic exudation, "not very dissimilar to the matter which forms on the inside of the trachea in croup," and in most of them, the heart has been flabby and fat, such a state of the arteries of the heart, must impair the function of that organ.

Burns classified diseases of the heart into three essential groups. The diseases of the first group were not detailed, but comprised those of a sympathetic nature or dependent on consent. It is probable that he was thinking in terms of functional disorders of the heart. The second group of diseases was composed of congenital defects and malformations which result in the admixture of arterial and venous blood. Burns, however, stressed the fact that cyanosis is not solely dependent on such admixture of blood. The third group of diseases was based on organic disease of the heart which mechanically interfered with the circulation of the blood but did not necessarily alter the properties of the blood.

Among the congenital cardiac anomalies, Burns described six basic types: cases in which the aorta arises from both the right and the left ventricle; those in which the foramen ovale and the ductus arteriosus are open; those in which the ductus arteriosus is closed but the foramen ovale is patent or a defect in the interventricular septum is present; those in which the pulmonary artery is closed at its origin but some blood gains entrance into the vessel from a patent ductus arteriosus; those in which the heart consists of only two chambers; and those in which a congenital stenosis of the mitral valve occurs.

Burns also described the symptoms and the pathologic findings in combined mitral and aortic disease and commented on atrophy of the heart, a rare condition previously observed by de Sénac. He also described unilateral paralysis of the diaphragm resulting from pressure on the phrenic nerve by a thoracic aneurysm. Burns described and discussed pericardial adhesions and stated that at times the pericardium was completely matted to the contiguous structures.

Prior to this time, only three references to the cardiac involvement occurring with rheumatism had been reported. In 1788 David Pitcairn discussed this relationship in a talk, but it was never recorded or published. A year later, Edward Jenner presented an oration before the Fleece Medical Society on the same subject but the manuscript was

lost and thus was never published. In 1797 Matthew Baillie casually mentioned the association of rheumatism and heart disease in the second edition of his work, "The morbid anatomy of some of the most important parts of the human body."

The first detailed report of this kind was contributed by William Charles Wells (1757–1817), who was born in Charleston, South Carolina. His father, a Scotsman, who had emigrated to the Colonies, sent his son to Edinburgh to obtain his preliminary education. After three and a half years, Wells returned to his home. Here he was apprenticed to Dr. Alexander Garden, the leading practitioner of Charleston. Dr. Garden was also interested in botany and zoology and became a correspondent of the famous Swedish botanist, Linnaeus, who perpetuated Garden's name by designating the beautiful flower which we know today as the gardenia.

The Wells family were strong supporters of the Crown and when the War of Independence broke out, they returned to England. Wells studied under the direction of John Hunter, spent some time at St. Bartholomew's Hospital, studied at Leyden for three months and then returned to Edinburgh, where he received his medical degree in 1780. He became a licentiate of the Royal College of Physicians in 1788, physician to the Finsbury Dispensary a year later and physician to St. Thomas' Hospital in 1800.

Wells's most important contribution, "On rheumatism of the heart," was read in 1810 and published in 1812. It must be remembered that these observations were made before the advent of auscultation, a fact which significantly increases their importance. Wells presented fourteen cases wherein he described the course of the rheumatic disease and stressed the symptoms of oppression in the chest, dyspnea, the occasional occurrence of hemoptysis and the presence of tachycardia and palpitation.

In 1792, Wells published a work on ophthalmology, "An essay upon single vision with two eyes; together with experiments and observations on several other subjects in optics," London, T. Cadell, 1792, 144 pp. Another important work of Wells appeared in 1814 which Pleadwell suggested was the basis for modern ventilation. This was published under the title, "An essay on dew, and several appearances connected with it," London, Taylor and Hessey, 1814, 146 pp. Another paper, "Account of a female of the white race of mankind part of whose skin resembles that of a Negro," appeared in his collected works in 1818. In 1811 Wells noted the appearance of albumin in the urine of patients suffering with dropsy.

It is of interest to note that early observations on coronary disease in the nineteenth century in America were recorded by two surgeons, father and son. In 1812, John Warren (1753–1815) of Roxbury, Massa-

chusetts, the first professor of surgery and anatomy at Harvard Medical School, had observed four cases of angina pectoris, in one of which postmortem examination had been performed. This was the case of a middle-aged clergyman who died several years after the onset of the painful seizures. The postmortem examination was conducted by Dr. Joshua Brackett, of Portsmouth, New Hampshire. Warren held the belief that "ossification" of the coronary arteries was not a prerequisite for the symptoms. In this case there were extensive pericardial adhesions and an increase in size of the coronary arteries. This observation led Warren to believe that other cardiac diseases were capable of producing painful seizures.

In 1813, John Collins Warren (1778–1856) also expressed skepticism regarding the relationship of disease of the coronary arteries and angina pectoris, for he had observed marked "ossification" of the coronary arteries in which angina pectoris was not present. Warren reported ten cases with postmortem findings, most of them instances of valvular disease and pericarditis in which death occurred in the presence of congestive heart failure. The first case reported was that of the colonial governor, Sullivan, who complained of oppression in the chest associated with dyspnea. Death occurred from congestive failure. At postmortem examination, the heart was found to be considerably enlarged and both aortic and mitral valvular disease were present.

It is evident that in the cases recorded, Warren did not encounter genuine instances of coronary disease.

John Richard Farre (1774–1862), of Glasgow, Aberdeen and London, observed congenital malformations and was apparently one of the first (in 1814) to describe the anatomic disarrangement consisting of pulmonary stenosis, dextroposition of the aorta, defect of the interventricular septum and hypertrophy of the right ventricle. William Hunter (1765), Gintrac (1824) and Peacock (1866) also observed this combination of anomalies but the first clear exposition of the condition did not appear until Fallot's publication in 1888. These defects today are known as the tetralogy of Fallot.

Friedrich Ludwig Kreysig (1770–1839), of Berlin, wrote an extensive work on the heart, "Die Krankheiten des Herzens," Berlin (1814–1817). Herrick, in discussing this work, stated that Kreysig added more confusion to the already existing confusion. His literary presentation was vague, owing to the fact that sentences of 100 to 300 words were frequently encountered and he appeared to have disregarded the use of the period.

Kreysig called attention to the systolic retraction of the left half of the epigastrium in cases of adherent pericarditis and mentioned the relation of rheumatism to endocarditis. He emphasized the fact that a heart showing marked pathologic changes at postmortem examina-

tion may have caused remarkably few symptoms while it was equally true that a heart showing few changes may have caused severe symptoms. Kreysig advocated the use of digitalis and called the drug a "God-given remedy." He believed spontaneous rupture of the heart to be of relatively common occurrence in spite of contradictory evidence. Kreysig described and discussed coronary sclerosis and commented on myocardial ischemia as the cause of angina pectoris.

Another physician who combined medicine and surgery was the prominent lithotomist, Joseph Hodgson (1788–1869), of Birmingham. His observations on the heart appeared in his widely used work, "Treatise on diseases of the arteries and veins," published in 1815. This work was well illustrated, gave the best descriptions of aneurysms of various types up to this time and contained the most accurate description of aneurysmal dilatation of the arch of the aorta. Examples of aortic endocarditis in varying stages were also depicted. His exposition of thoracic aneurysm was so impressive to the French physicians that they frequently referred to the disease as the *"maladie d' Hodgson."*

Friedrich Ludwig Kreysig.

Hodgson described a case of angina pectoris attended by sudden death in which postmortem examination revealed marked calcification of a main coronary artery and softening of the myocardium in the region supplied by this artery to such a degree that a finger could readily be thrust through the musculature. Without knowing the true meaning of his findings, Hodgson undoubtedly observed acute myocardial infarction with necrosis of tissue.

An important contribution was made by John Cheyne (1777–1836), of Edinburgh and Dublin. A graduate of the University of Edinburgh in 1795, he became assistant surgeon of the medical corps of the Royal Regiment of Artillery and two years later was promoted to the rank of surgeon. Cheyne was in action against the rebels in Ireland in 1798. He left the army a year later and entered private practice in Scotland where he remained ten years and then established practice in Dublin. In 1811 he was appointed physician to the Meath Hospital and soon was invited to lecture at the Irish College of Surgeons. In 1815 he was appointed to the staff of the House of Industry.

Cheyne was the first to describe that periodic type of breathing later to be known as Cheyne-Stokes respiration. William Stokes (1804–1878) gave a fuller description of this phenomenon in 1854 and called attention to its diagnostic significance. Cheyne reported his findings, in the case of a patient with fatty heart, in his article, "A case of apoplexy, in which the fleshy part of the heart was converted into fat," 1818.

Other publications of Cheyne included his doctoral thesis, "De rachitide," 1795 and several articles on diseases of children.

No doubt exists that the most important contribution of the first half of the nineteenth century to cardiology was the discovery of auscultation by René-Théophile-Hyacinthe Laënnec (1781–1826), of Paris (see special biography). The discovery of auscultation and its application as a practical method of diagnosis, particularly in diseases of the heart and lungs, provided physicians with a new diagnostic procedure which gave prompt impetus to notable progress. With the discovery of auscultation, the tetralogy of physical diagnosis, inspection, palpation, percussion and auscultation, became complete.

John Cheyne.

Laënnec's famous work, "Traité de l'auscultation médiate," was published at Paris in 1819. In this work, he quoted his famous teacher, Corvisart, extensively. The contents of the book are remarkably comprehensive and recurrently call attention to the utilization of the four components of physical diagnosis.

Laënnec correctly recognized that the first heart sound coincided with systole of the ventricle but erroneously believed that the second heart sound occurred with systole of the auricle. He referred to the palpable thrill as *frémissement cataire* (the purring of a cat) and recognized venous hums. In reading Laënnec's work one is impressed by the remarkably modern theme that prevails in certain sections, particularly where he discusses "fatty degeneration of the heart." The discussion of valvular defects, endocarditis, carditis, pericarditis and so forth is of unusual interest.

Laënnec, like many of his contemporaries, had little understanding of angina pectoris. In commenting on symptoms common to all diseases of the heart, he wrote, "To these symptoms is frequently added the

angina pectoris,—a nervous affection characterized by a sense of oppression, a constriction and oppression in the region of the heart, and a pain or numbness of the arm, more commonly the left, sometimes of both at once." He was one of the pioneers in the clinical recognition of thoracic aneurysm.

An early description of complete heart block was contributed by Sir William Burnett (1779–1861), of Montrose, Edinburgh and Chichester. He was a British naval officer who later became Physician General to the Royal Navy, a post comparable to that of the Surgeon General of the United States Navy. Burnett reported a case of complete heart block with convulsive syncope under the title, "Case of epilepsy, attended with remarkable slowness of the pulse," which was published in Medical and Chirurgical Transactions, London (13:202–211, 1827). This paper, however, had been read in 1824.

Robert Adams.

This account of heart block was written 105 years after that of Gerbezius but preceded the descriptions of Adams and Stokes by three and thirty years respectively.

Reports concerning congenital anomalies of the heart appeared more frequently and physicians were becoming more conscious of these defects as entities and were attempting to recognize them during the life of the patient. Élie Gintrac (1791–1877) of France was another to describe the combination of congenital anomalies later to be known as the tetralogy of Fallot (pulmonary stenosis, dextroposition of the aorta, patency of the interventricular septum and hypertrophy of the right ventricle). These observations were reported in his treatise, "Observations et recherches sur la cyanose ou maladie bleue," Paris, 1824. Gintrac's report followed Farre's by ten years but preceded Fallot's by sixty-four years.

The fifth recorded report of the hitherto rare condition, complete heart block, was published by Robert Adams (1791–1875), of Dublin. He was one of the outstanding physicians of Ireland who made numerous important and interesting contributions to medicine. In 1815, Adams was licensed by the Royal College of Surgeons in Ireland, and in 1818, at the age of twenty-seven years, was elected to full membership. His first appointment was at the Jervis Street Hospital where Adams and

John McDowell ultimately succeeded the celebrated Richard Carmichael. Adams was the cofounder of two medical schools; the first, the Peter Street School of Medicine, was founded in collaboration with Kirby and Read, and the second, at the Richmond Hospital, named the Carmichael School of Medicine and Surgery, was founded in association with Carmichael and McDowell. While teaching at this latter school, Adams produced most of his works.

Adams' account of heart block associated with convulsive syncope, later to become known as the Adams-Stokes syndrome, appeared under the title, "Cases of diseases of the heart, accompanied with pathological observations," in the Dublin Hospital Reports, 1827. In the case reported, Adams commented particularly on the fatty changes found in the heart and referred to the similarity of findings to those in the case reported by Cheyne in 1818 in which the peculiar respiratory phenomena had been noted. Adams also commented on the extreme thinness of the left ventricle. Although he did not realize the implications of this observation, it may well have represented a region of healed or partially healed myocardial infarction. However, he made no remarks regarding the state of the coronary arteries.

In order to maintain the historic chronology of accounts dealing with heart block, a brief statement of their order appears important. The first instance of heart block was recorded by Gerbezius in 1719, Morgagni's case was reported in 1761, Spens's case in 1793 and Burnett's in 1824. William Stokes's publication did not appear until 1854.

In other publications, Adams discussed mitral and aortic stenosis and obliterative sclerosis of the coronary arteries. He observed pericardial adhesions in enlarged hearts and expressed the interesting view that the enlargement of the heart resulted from increased vascularity through the adhesions from sources outside of the heart. Adams held the belief that the valves of the left side of the heart were more subject to disease than those of the right side because their closure was more perfect. The same view had been expressed by John Hunter nearly a half century earlier. Adams evidently possessed a remarkably advanced concept regarding certain mechanics of heart failure for he contended that the development of regurgitation at the tricuspid valve relieved stasis in the pulmonary circulation.

Adams wrote extensively on abnormalities of the joints. This work appeared in Todd's "The cyclopaedia of anatomy and physiology," London, 1835–1859. In 1857 he published his classic account of gout, "Treatise on rheumatic gout, or chronic arthritis of all the joints," London, J. Churchill, 302 pp.

Both important and interesting contributions dealing with the heart and arteries were made by Thomas Hodgkin (1798–1866), of Tottenham and London. He was a capable clinician and an outstanding path-

ologist. Hodgkin was elected to membership in the College of Physicians, London, in 1825 and soon thereafter spent considerable time in France and Italy. On his return to England, he became associated with Guy's Hospital in the capacity of curator of the museum of pathology and demonstrator in this field. Hodgkin applied himself vigorously to this task and collected an enormous amount of material which formed the basis of many of his subsequent works.

Hodgkin described arteriosclerosis and made the first concerted attempt to classify the arterial lesions which he observed. He recognized three types, those that were cartilaginous, those that were pulpy and those that were purulent. This classification appeared in his work, "On diseases of arteries and veins." Hodgkin presented an excellent description and account of insufficiency of the aortic valve, which preceded Corrigan's classic description by three years. This article, "On retroversion of the valve of the aorta," appeared in the London Medical Gazette (3:433, 1828–1829). Hodgkin called attention to the to-and-fro murmurs and commented on the full bounding pulse, stating that at times the patient's head was seen to move in concert with the beat of the heart.

Thomas Hodgkin.

Hodgkin described and illustrated instances of aneurysms and aneurysmal dilatation of the aorta. He was the first to observe that the vegetations in acute rheumatic endocarditis were located near but not at the edges of the valve leaflets and called attention to the implantation of acute vegetations by contact of the valve leaflet with the adjacent endocardium.

Hodgkin's name is immortalized by his description in 1832 of the disease characterized by enlargement of the lymph nodes and frequently of the spleen (lymphoblastoma), which Sir Samuel Wilks (1824–1911) named Hodgkin's disease in 1865. In 1823 he published a treatise on medical education and his famous "Lectures on the morbid anatomy of the serous and mucous membranes" (1836–1840) constituted one of the earliest English treatises on pathology. Among many subjects it included a discussion of acute appendicitis and its complications.

An attempt to improve on Auenbrugger's method of percussion was

undertaken by Pierre-Adolphe Piorry (1794–1879), of Poitiers, who invented the pleximeter. The description of his method and instrument appeared in his work, "De la percussion médiate," Paris, in 1828. Piorry had devised the pleximeter two years earlier. This method of percussion, however, was not widely accepted and never became a universally acknowledged procedure.

An early record of pericardial incision for effusion was made by the eminent French military surgeon, Dominique-Jean Larrey (1766–1842). A student of the celebrated Antoine Louis (1723–1792) and Pierre-Joseph Desault (1744–1795), he became one of Napoleon's favorite surgeons. Napoleon bequeathed 100,000 francs to Larrey with the comment that he was the most virtuous man he had ever known. Larrey was chief surgeon to the *Grande Armée*, participated in sixty battles and was wounded three times.


Dominique-Jean Larrey.

In 1829 he reported his case of pericardial section. The following quotation is from the review of Ballance.

> Larrey's patient was a man, aged 30, who stabbed himself with a knife in the left side of the chest; the pericardium and the left lung were wounded, the knife had passed through the fifth costal cartilage and was still in the wound when he was brought to the hospital. Frothy blood escaped in jets with each systole. The knife was withdrawn and the wound dressed with plaster; the patient tore off the dressing and it was reapplied. The pulse was rapid and there was grave dyspnoea. Bleeding gave some relief. Some improvement took place, but later on he became worse, and in great distress requested Larrey either to open his chest or to give him a narcotic strong enough to send him to sleep. Operation 45 days after injury, incision through skin and cellular tissue in fifth space below nipple, carefully carried deeper until pericardium was felt. With the left index finger on the pericardium as a guide an incision into the pericardium was made with a bistoury, the finger inserted, and the apex of the heart felt. About a litre of fluid with some blood clot escaped. Great relief. In ten days the wound closed and the symptoms recurred. Wound reopened with a probe, 4 oz. of pus escaped. Considerable improvement. Death 68 days after injury and 23 after operation. Autopsy: Suppurative mediastino-pericarditis.

Larrey conducted experiments on the cadaver, performing stab wounds and noting their direction and points of entry into the heart. He advocated the epigastric approach to the pericardium, as he believed this permitted access to the most dependent portion of the pericardial sac.

He is said to have performed 200 amputations within twenty-four hours, introduced ambulances to remove the wounded from fields of battle and was the originator of the modern concept of "first-aid treatment." Soon after the establishment in 1796 of the École de médecine militaire at Val-de Grâce, Larrey became professor of surgery there.

The earliest attempt to obliterate the sac of aneurysms by the production of mural thrombosis was that of Alfred-Armand-Louis-Marie Velpeau (1795–1867), of Paris. He became surgeon to the Hôpital St. Antoine, La Pitié and Charité and was professor of surgery of the Paris Faculty from 1834 to 1867.

In 1830 Velpeau suggested the insertion of needles into the aneurysmal sac with the intent of producing local irritation with consequent formation of a thrombus. His work appeared as "Mémoire sur la piqûre ou l'acupuncture des artères dans le traitement des anévrismes."

Alfred-Armand-Louis-Marie Velpeau.

Two years later, Benjamin Phillips (1805–1861), of London, employed the same method. His work was published under the title "A series of experiments for the purpose of showing that arteries may be obliterated without ligation, compression or the knife," London, 1832.

An American pioneer in vascular surgery was Valentine Mott (1785–1865), of Long Island, a student of Sir Astley Paston Cooper. Mott ligated the innominate artery for the first time in 1818 but the operation was not successful. However, in 1827 he successfully ligated the common iliac artery at its origin, the carotid artery for aneurysm in 1829, the carotid artery for hemangioma in a three month old infant in the same year, the external iliac artery for femoral aneurysm in 1831, the right subclavian artery in 1833, both carotids simultaneously in the same year and the right internal iliac artery in 1837. All told, Mott ligated great arteries for aneurysm 138 times.

These were amazing accomplishments in Mott's day and age and clearly demonstrated his heroic courage after initial failure.

Apparently the first to describe arteriosclerosis of the pulmonary artery was Gabriel Andral (1797–1876), professor of general pathology at Paris. Many of his observations were published in his work, "Clinique

médicale," published from 1829 to 1833. In his discussion of acute fibrinous pericarditis, Andral considered the painful symptoms of the disease and called attention to the fact that the pain at times simulated that of angina pectoris.

Andral edited the works of Laënnec. He did much to establish the science of hematology and contended that primary disease of the blood existed. These observations and conclusions were published in 1843 in his "Essai d'hématologie pathologique," Paris.

A successful practitioner of Edinburgh and London, James Hope (1801–1841), made important contributions to the knowledge of diseases of the heart and aorta. An Edinburgh graduate in 1825, the topic of his thesis was "Aneurism of the aorta."

A year later, Hope, desirous of receiving graduate training, went to London where he studied surgery at St. Bartholomew's Hospital. Later in the same year he successfully passed his examinations before the College of Surgeons in London. The ensuing year was spent in Paris where he studied under Dr. Auguste-François Chomel. In 1827, he studied in Switzerland and Italy and at the close of the year established his practice in London.

James Hope.

Hope died at the age of forty years but his short career was filled with accomplishments. His classic work, "A treatise on the diseases of the heart and great vessels," was published in 1831. This work was republished in numerous editions and the first American printing appeared in 1842.

Interested in the mechanism of production of the heart sounds, Hope experimented on donkeys. He examined the hearts of stunned donkeys the respiration of which had been artificially sustained after the pericardium was opened and proved that the second heart sound is dependent on the abrupt closure of the aortic and pulmonary valves.

Hope described the physical signs of aortic, mitral and pulmonary valvular stenosis and aortic insufficiency. Incidentally, his work was the first standard textbook to describe the diastolic murmur of aortic insufficiency. Hope also postulated the signs that should attend stenosis of the tricuspid valve and further described the systolic murmur of

mitral insufficiency. He described cardiac asthma and wrote interestingly on cardiac neurosis. The following brief quotation from this section of his work is of interest:

> There are few affections which excite more alarm and anxiety in the mind of the patient than this. He fancies himself doomed to become a martyr to organic disease of the heart, of the horrors of which he has an exaggerated idea; it is the more difficult to divest him of this impression because the nervous state which gives rise to his complaint, imparts a fanciful gloomy and desponding tone to his imagination.

Hope attempted to classify the symptoms and signs of congenital anomalies of the heart and called attention to the diagnostic value of the doubling of the apex beat, or "double jogging" as he called it, in cases of thoracic aneurysm. He also noted pericardial adhesions and commented on their limiting effect on the movements of the heart. Hope advised the restriction of fluid intake of patients exhibiting anasarca.

Sir Dominic John Corrigan.

Another stalwart of the great Irish school of medicine was Sir Dominic John Corrigan (1802–1880), of Dublin, who became professor of medicine at the Digges Street School and later served in the same capacity in the Peter Street School and in the Carmichael School. A graduate of the University of Edinburgh in 1825, he was a classmate of the eminent William Stokes. Corrigan presented the clearest and most accurate account of aortic insufficiency up to his time, although accounts had already been published by Vieussens (1695), Cowper (1705) and Hodgkin (1828–1829). Corrigan's classic article appeared under the title, "On permanent patency of the mouth of the aorta, or inadequacy of the aortic valves," in the Edinburgh Medical and Surgical Journal, 1832.

In this publication, Corrigan discussed the origin of the diastolic murmur and clearly described and discussed the characteristic bounding or "water-hammer" pulse of aortic insufficiency which, even today, is frequently referred to as the Corrigan pulse. In 1829 he published an article, "An aneurism of the aorta," which appeared in the Lancet. In this work he emphasized the value of auscultation in the clinical recognition of aneurysm of the thoracic aorta. In another article published in the same journal a year later, "Inquiry into the causes of 'bruit

de soufflet' and 'frémissement cataire,'" he corrected Laënnec's beliefs that these phenomena were not the result of spasm but were on the basis of organic valvular changes.

Another important article by Corrigan, "On aortitis as one of the causes of angina pectoris," appeared in the Dublin Journal of the Medical Sciences in 1837. A year later, in the same journal, he published his famous article on cirrhosis of the lung (fibroid disease of the lung), a disease which the great French clinician, Armand Trousseau, named "maladie de Corrigan" or "Corrigan's cirrhosis."

Following the publication of Corrigan's account of aortic insufficiency, which he thought had been the first to appear, James Hope violently opposed the claim to priority and contended that he had lectured on the subject as early as 1825.

Like others of his era, Corrigan decried the use of digitalis in cases of aortic insufficiency.

Jean Cruveilhier.

A generous contributor to the ever-increasing knowledge of pathology was Jean Cruveilhier (1791–1873), of Paris. His intention to study for the priesthood, when he became shocked at witnessing a postmortem examination during his early medical career, was frustrated by his father's firm attitude and determination that he continue with his medical studies. Cruveilhier was a student of the famous French surgeon Dupuytren and graduated at Paris in 1816. Through the influence of this teacher, Cruveilhier was appointed professor of surgery at Montpellier in 1823 and two years later he accepted the post of professor of descriptive anatomy at Paris. In 1836 he became the first professor of pathology of the Paris Faculty and held this office for the remarkably long period of thirty years.

Cruveilhier's famous work on pathology, a superbly illustrated atlas, was titled "Anatomie pathologique du corps humain" and was published from 1830 to 1842. He presented colored reproductions of myocardial infarcts but did not ascribe the changes noted to disease of the coronary arteries. Cruveilhier contended, however, that they did not represent fatty metamorphosis. Among many pathologic notes were descriptions of gastric ulcer and here he called attention to recurrent hemorrhages which at times proved fatal.

Cruveilhier held the erroneous belief that phlebitis governed all pathologic processes. He did not employ microscopy and many of his errors were later corrected by Virchow.

A celebrated French physician, René-Joseph-Hyacinthe Bertin (1767–1828), of Paris, contributed to the knowledge of diseases of the heart. His medical education was obtained at Paris and Montpellier and he received his medical degree from the latter university in 1791. After serving as an army medical officer, Bertin was appointed physician-in-chief at the Cochin Hospital and later succeeded Hallé as professor of hygiene at the Hospital for Venereal Diseases.

Bertin's outstanding work, "Traité des maladies du coeur et des gros vaisseaux," was published in Paris in 1824. He described valvular vegetations and valvular deformities with special reference to their signs, described the presystolic murmur of mitral stenosis and gave an excellent account of atrophy of the heart. Bertin was greatly interested in the problem of cardiac hypertrophy and by means of microscopy demonstrated an actual increase in the amount of musculature. He classified hypertrophy of the heart into three types, concentric, excentric and simple. This classification prevailed in medical literature for many years.

Another ranking pathologist of this period was Johann Friedrich Lobstein (1777–1835), the first professor of pathology of the then French University of Strasbourg. While pre-eminently interested in pathology, he integrated the functions of organs in his lectures and writings and is said to have introduced the term "pathogenesis." In 1833, Lobstein presented an unusually accurate description of arteriosclerosis. His outstanding work, "Traité d'anatomie pathologique," published at Paris in 1829, was never completed.

One of the most outstanding French physicians of this era was Jean-Baptiste Bouillaud (1796–1881), of Angoulême and Paris. He was a Paris graduate in 1823 and among his teachers were such notables as Guillaume Dupuytren, François-Joseph Broussais, Jean-Nicolas Corvisart and François Magendie. Bouillaud's internship was served at the Cochin Hospital under René-Joseph-Hyacinthe Bertin. In 1825, at the age of twenty-nine years, he became a member of the Académie de Médecine and a year later was named assistant professor of the Paris Faculty. In 1831, he succeeded Joseph Récamier as professor of clinical medicine.

In 1835, Bouillaud published his "Traité clinique des maladies du coeur," which among many subjects contained his classic description of endocarditis. While endocarditis and valvular defects had frequently been mentioned and described in the past, Bouillaud's account was the most advanced yet to appear. He divided endocarditis into three phases or stages. The first stage was that "of sanguinary congestion, of softening and of ulceration or suppuration." Medical knowledge of this era

did not afford physicians the understanding of the subject that later bacteriologic investigations made possible and the differentiation of etiologic types of the disease was unknown although the relation of rheumatism to endocarditis and heart disease in general had been noted. In this first stage of endocarditis, Bouillaud evidently included acute endocarditis of all types. In his second stage, he included cases in which "organization of secreted products or of a portion of fibrinous concretions" occurred. This would undoubtedly represent instances of subacute endocarditis. Finally the third stage or chronic and healed phase of the disease represented that "period of cartilaginous, osseous or calcareous induration of the endocardium in general and of the valves in particular, with or without narrowing of the orifices of the heart."

In 1836 Bouillaud published his work, "Nouvelles recherches sur le rheumatisme articulaire," Paris. In this volume he irrevocably established the etiologic relationship between rheumatic fever and heart disease. Earlier reports on this relationship had been contributed by Pitcairn, Jenner and Wells, but Bouillaud's exposition was more authoritative, comprehensive and accurate than theirs. He amplified these observations in a subsequent work, "Traité clinique du rheumatisme articulaire," Paris, published in 1840.


Jean-Baptiste Bouillaud.

Bouillaud also contributed the "law of coincidence," which in translation is stated in the following words: "In the great majority of cases of acute generalized febrile articular rheumatism, there exists a variable degree of rheumatism of the fibrous tissue of the heart. This coincidence is the rule and the non-coincidence the exception."

In the second edition of his work, "Traité clinique des maladies du coeur," published in 1841, Bouillaud devoted considerable attention to the measurements and weights of hearts. According to Rolleston, these were the first accurate studies of this nature. He also described the split second heart sound and attributed it to asynchronism in closure of the aortic and pulmonary valves. Bouillaud described the "bruit de diable," a venous humming sound heard over the internal jugular vein in chlorosis and the "bruit de rappel," which represented the false reduplication of the second sound of the heart at the apex

in mitral stenosis. He was of the opinion that congenital cardiac anomalies were caused both by inherent defects of development and by disease of the fetus. Bouillaud insisted that myocarditis occurred independently of endocarditis and pericarditis. He stated that digitalis was the "opium of the heart." Bouillaud was a prodigious blood-letter, although not as radical as his predecessor and teacher, Broussais, who exceeded all previous and subsequent records. Bouillaud favored very rapid bleeding, which was referred to as *"coup sur coup."*

He also contributed to neurology. His most important contribution in this field was his identification of the anterior lobes of the brain as the center of speech. In 1827, Bouillaud published two articles refuting Franz Gall's (1758–1828) ideas concerning the function of the cerebellum. Gall held the view that the cerebellum had to do with the instinct of propagation while Bouillaud presented evidence that this portion of the brain was the organ of equilibration, station and progression. He also showed that lesions of the cerebellum affected co-ordinate movements.

Richard Bright.

Further clinical discrimination regarding the timing, character and significance of murmurs in relationship to cardiac valvular defects became more evident. Laënnec's introduction of auscultation earlier in the century had made this method of clinical detection widespread in its application, notably by the physicians of the British Isles. Charles J. B. Williams (1805–1889), a prominent English physician, was an authority on "consumption" and diseases of the thorax.

Williams gave the first complete description of the murmurs of mitral stenosis in his work, "Diseases of the chest," London (Ed. 3, 1835). Bertin and others, however, had discussed the presystolic murmur earlier. Williams particularly emphasized the diastolic murmur of mitral stenosis and contended that it was not produced by the semilunar valves, because they were normal. He was of the opinion that the first sound of the heart was produced by muscular contraction because in an experiment on the heart of an ass from which the blood had been removed, the first sound was still audible during cardiac systole. He reasoned erroneously that under these circumstances the valve leaflets did not move.

Williams also described paroxysmal tachycardia and reported the successful surgical closure of a stab wound of the heart.

One of the most brilliant English physicians and teachers of this century was Richard Bright (1789–1858), of London. An Edinburgh graduate of 1813, he was physician to Guy's Hospital for twenty-three years and was associated with such illustrious men as Addison and Hodgkin. Bright performed many postmortem examinations and, in addition to teaching pathology, also taught clinical medicine and materia medica. An accomplished artist and a great lover of art, Bright used this talent both in teaching and in the illustration of some of his writings.

Bright's most outstanding contributions dealt with the kidney but were closely integrated with the pathology of the cardiovascular system. He established the nature of nephritis (Bright's disease). This famous work was published in "Reports of medical cases selected with a view of illustrating the symptoms and cure of diseases by a reference to morbid anatomy," London (vol. 1, 1827). In these writings, he presented his original and classic description of nephritis and distinguished between renal dropsy and dropsy from other causes. The following brief quotations are of interest:

> . . . One great cause of dropsical effusion appears to be obstructed circulation; and whatever either generally or locally prevents the return of the blood through the venous system, gives rise to effusion of serum more or less extensive. Thus, diseases of the heart which delay the passage of the blood in the venous system, give rise to general effusion, both into the cavities and into the cellular tissue. Obstructions of the circulation through the liver, by causing a delay in the passage of the blood through the veins connected with the vena portae, give rise to ascites. The pressure of tumours within the abdomen preventing the free passage of blood through the vena cava gives rise to dropsical effusion into the cellular tissue of the lower extremities: and not infrequently, the obliteration of particular veins from accidental pressure is the source of most obstinate anasarcous accumulation.
>
> . . . There are other appearances to which I think too little attention has hitherto been paid. There are those evidences of organic change which occasionally present themselves in the structure of the *kidney;* and which, whether they are to be considered as the cause of the dropsical effusion or as the consequence of some other disease, cannot be important. . . .

In 1836, Bright described cardiac hypertrophy in association with contraction of the kidney in the absence of cardiac valvular disease. He discussed the etiologic relation of chorea, in the absence of rheumatic fever, to endocarditis and pericarditis. He gave accurate accounts of diabetes mellitus and pancreatic steatorrhea in 1832, of acute yellow atrophy of the liver in 1836, and of status lymphaticus in 1838.

John Calthrop Williams (nineteenth century), of Edinburgh, a physician and lecturer at the Nottingham Union Hospital and Dispensary, wrote a treatise on nervous and sympathetic palpitation of the heart. While Hope's account of nervous palpitation had appeared five years earlier (1831), this subject then as today demanded emphasis and reiteration. Williams' book, "Practical observations on nervous and

sympathetic palpitation of the heart, particularly as distinguished from palpitation the result of organic disease; to which are prefixed some general remarks on the use of the stethoscope and employment of percussion in diagnosis of diseases of the heart and lungs," London, appeared in 1836.

In this book, Williams called attention to the fact that nervous disorders of the heart were too frequently confused with organic disease. The following quotation from Williams' work is strikingly to the point: "No man, I am satisfied, can ever be a sound Pathologist, or a judicious practitioner, who devotes his attention to one of these systems in preference or to the exclusion of the other; through life they are perpetually acting and inseparably linked together."

Probably the greatest master in the science and art of physical diagnosis was Joseph Skoda (1805–1881) of Pilsen and Vienna (see special biography). He was the greatest of all the famous clinicians of the new Viennese school of medicine which rose to prominence near the half century mark. Skoda was an intelligent observer and an inspiring teacher who developed an amazing ability to solve obscure diagnostic problems by the adroit use of inspection, palpation, percussion and auscultation. A Vienna graduate in 1831, Skoda captured the admiration and respect of his superiors when he correctly identified the illness of the Duc de Blacas, French minister to Austria. Such outstanding physicians as Malfatti, Türkheim and Wirer had made the diagnosis of disease of the liver but Skoda's diagnosis of aneurysm of the abdominal aorta was verified at postmortem examination. Thereafter, Türckheim became greatly interested in young Skoda. He was appointed physician to the Allgemeines Krankenhaus, where he taught medicine for many years and was the first to deliver lectures there in the German language.

Skoda's outstanding work, "Abhandlung über Perkussion und Auskultation," Vienna, was published in 1839. In this work he reaffirmed Auenbrugger's observations and carried them to a greater degree of refinement and significance. He emphasized the belief that each disease displayed a specific set of signs and insisted that the sounds of percussion depended on the underlying physical conditions and that all observation must be reconciled with the laws of acoustics.

Skoda described a tympanitic sound heard on percussing the thorax above the level of a massive pleural effusion or above a pneumonic consolidation, which still today is known as Skoda's sign. He taught that the apex beat of the heart was produced by the recoil of the heart which resulted from the column of blood projected into the aorta.

Skoda is said to have been the originator of the so-called therapeutic nihilism which characterized this era of Viennese medicine, although this was probably not true. The establishment of a diagnosis and its confirmation at postmortem examination apparently superseded therapeutic interest and effort.

Outstanding contributions in the fields of histology and physiology were made by Johannes Evangelista Purkinje (1787–1869), of Breslau and Prague. A graduate of Prague in 1819, his thesis on subjective visual phenomena was widely acclaimed and won for him early recognition. This work was published the same year under the title, "Beiträge zur Kenntniss des Sehens in subjectiver Hinsicht," Prague. This contribution resulted in his close friendship with Goethe, who aided him in securing the professorship of physiology and pathology at the University of Breslau in 1823. He held this post for twenty-seven years, when he accepted the professorship of physiology at Prague.

Purkinje founded the laboratory training of students and in 1842 the Prussian government erected a Physiologic Institute in Breslau. His discovery relating to the heart rested in the demonstration of the terminal fibers of the conducting system in the subendocardial layer of the myocardium. These structures today are known as the Purkinje fibers. This important work unfortunately was not recorded in medical literature under Purkinje's authorship but was published by one of his students with full credit to the master. The student, Bogislaus Palicki, published the findings in his treatise, "De musculari cordis structura," Breslau, 1839.

Johannes Evangelista Purkinje.

Purkinje also described the visual manifestations of digitalis intoxication. He was the first to use the microtome and was the originator of special methods of tissue fixation. In 1825, Purkinje described the germinal vesicle in the embryo in his article, "Symbolae ad ovi avium historiam ante incubationem," Breslau. He was the first histologist to use the term "protoplasm" and he discovered the sudoriferous glands of the skin and their ducts in 1833. In 1837, Purkinje discovered the ganglionic cells of the cerebellum which bear his name and the lumen of the axis cylinder of nerves. In collaboration with Gabriel Valentin, he published the famous treatise on ciliary epithelial motion in 1834–1835. He further discussed the value of finger prints in identification of persons and demonstrated that deaf mutes were sensitive to vibrations conducted by the bones of the skull. These are but a few of this great man's accomplishments.

Marshall Hall (1790–1857), of Nottingham and London, was a successful practitioner of medicine and was interested in physiologic experimentation, particularly with reference to the central nervous system. His contribution with reference to the heart lies in his contention that sudden death is often related to stoppage of the coronary circulation. This appeared in his work, "The mutual relations between anatomy, physiology, pathology, and therapeutics, and the practice of medicine," London, 1842.

His Royal Society memoir on "The reflex function of the medulla oblongata and medulla spinalis" was published in 1833 and demonstrated the difference between volitional action and unconscious reflexes. Hall proved that the convulsions produced by strychnine are abolished on destruction of the spinal cord, that reflex phenomena are more readily produced by stimulation of the nerve endings than by direct stimulation of the nerves and that a reflex mechanism exists in sphincter muscles.

Marshall Hall.

One of the earliest experiments with reference to the coronary circulation was performed by John E. Erichsen (1818–1896), of London. An eminent surgeon of Danish extraction, he was personal physician to Queen Victoria and ultimately was knighted. Erichsen ligated the coronary arteries of dogs and rabbits and found that death of the animals occurred within ten minutes. He concluded from these experiments that any disease, such as "ossification" of the coronary arteries, that interferes with the flow of blood through them may result in sudden death. These experiments were published in his article, "On the influence of the coronary circulation on the action of the heart," London Medical Gazette, 1842.

Important observations on pericarditis were recorded by Norman Chevers (1818–1886), of London. He held remarkably advanced views on the form of pericarditis which today is known as "constrictive pericarditis." Chevers' work appeared in an article titled, "Observations on the diseases of the orifice and valves of the aorta," in Guy's Hospital Reports (5:387, 1842). In this article he discussed the compression effects of pericardial adhesions and the manner in which they restricted

both systole and diastole of the heart, emphasizing particularly the interference with diastole.

Chevers believed that, when cardiac enlargement accompanied the occurrence of pericardial adhesions, some other cause for the enlargement must be sought, such as valvular lesions. In fact he was of the opinion that constriction of the heart was capable of producing atrophy of the organ.

Chevers expressed the opinion that the physical signs accompanying stenosis of the aortic valve could appear in the absence of aortic disease. He observed vegetations situated on the interventricular septum near the attachment of the aortic cusp of the mitral valve which gave rise to signs simulating the aforementioned valvular defect. Chevers was the first to demonstrate insufficiency of the pulmonary valve at postmortem examination.

Sir John Erichsen.

As the nineteenth century advanced, recorded observations showed the ever-increasing benefits which were accruing from Laënnec's discovery of auscultation. The auscultatory evidence of valvular lesions became more precise and the correlation of these clinical findings with postmortem revelations furnished the conclusive proof of their correctness. The publication of Sulpice-Antoine Fauvel (1813–1884), of Paris and Constantinople, was another example of this type of diagnostic effort. He was a Paris graduate in 1840 and capillary bronchitis was the subject of his thesis. Fauvel became chief-of-clinic at the Hôtel Dieu but in 1847, owing to the ravages of the plague, he was called to an important post in Constantinople.

He became a member of the Imperial Council of State of the Ottoman Empire, in 1849 was appointed professor of medicine at Constantinople and six years later founded the Gazette Médicale d'Orient.

While still in Paris, Fauvel published his interesting account of the signs of mitral stenosis. We are indebted to Major for his translation and reproduction of this article. This work appeared under the title, "Communication concerning the stethoscopic signs of narrowing of the left auriculo-ventricular orifice of the heart," (translation) in Archives générale de médecine, Paris, 1843. The following is a brief

quotation from Major's translation: "In the precordial region, besides a forceful impulse and a considerable area of dullness, one heard an *intense rasping murmur (bruit de râpe), preceding the first sound, finishing with it,* having its maximum intensity at the apex of the heart and to the left."

One of the pioneers in the field of electrophysics was Carlo Matteucci (1811–1868), of Forlì, a student of Müller. Already toward the close of the eighteenth century, another celebrated Italian, Luigi Galvani (1737–1798), professor of anatomy at Bologna, had made important observations on animal electricity. As the results of his experiments paved the way for Matteucci and others who were to follow, a brief discussion of Galvani's work at this point appears important. One day while working in his laboratory, Galvani had placed a dissected frog on a table near an electric machine. His assistant had touched the nerves of the frog's leg with a knife, and the leg contracted vigorously. Galvani, greatly interested in this phenomenon, investigated this strange behavior and ultimately discovered that the leg would contract when the nerve was touched only when the electric machine was sparking. In many later experiments, Galvani studied the effects of electrical stimulation of muscles.

Norman Chevers.

Matteucci placed the central end of the severed peripheral segment of the sciatic nerve of one leg of a frog on the muscles of the opposite leg. When the sciatic nerve of the intact side was stimulated, the muscles of both legs contracted, although only the intact side had been stimulated. This important experiment in electrophysics was published in his article, "Sur le courant électrique des muscles des animaux vivants ou récémment tués," Comptes Rendus des Séances de l'Académie des sciences (16:197, 1843).

The following quotation is from White's translation of Matteucci's article:

1. The signs of the electrical current of the frog itself, demonstrated by the galvanometer, increase in the same instrument in the act of contraction. . . . 2. *The muscular electrical current,* which I shall hereafter call the muscular current, is present in all muscle masses, whatever the animal. I have taken pectoral muscles

of pigeons, a rabbit's back muscles, hearts of pigeons. . . . In all cases I have obtained a current which flows from the interior of the muscle to the surface. . . .

While these observations were only indirectly related to the heart, they nevertheless were important forerunners of the eventual development of electrocardiography. The galvanometer had been invented by Johannes S. C. Schweigger (1779–1857), of the University of Halle.

As already emphasized from time to time in the discussion of this era, much confusion existed regarding the cause of angina pectoris and its relation to disease of the coronary arteries. Even in spite of the convincing studies of Allan Burns and others, subsequent writers continued to complicate the subject. John Forbes (1787–1861), of London, added more confusion to the existing bewilderment in his publication which appeared in the "Cyclopedia of practical medicine," 1845. He contended that in approximately half of the cases of angina pectoris, no organic disease of the heart existed while in the other half a great variety of cardiac and especially aortic lesions occurred.

John Forbes.

A pioneer in neurophysiology, Ernst Heinrich Weber (1795–1878), of Wittenberg, was professor of anatomy and physiology at Leipzig from 1821 to 1866 and was succeeded in physiology by Carl Ludwig and in anatomy by Wilhelm His. In collaboration with his brother, Eduard Friedrich Weber (1806–1871), also an anatomist and physiologist, he made the important discovery proving the cardio-inhibitory action of the vagus. Their ingenious experiment consisted in placing one pole of an electromagnetic apparatus in the nostril of a frog and placing the other pole on a cross section of the spinal cord at the level of the fourth vertebra. On stimulation, this procedure resulted in standstill of the heart. In their analysis of the field of inhibition, which they localized between the optic lobes and the calamus scriptorius, the Weber brothers found the vagi to be the communicating pathways.

These experiments were reported at a meeting of the Congress of Italian Scientists in Naples and were published under the title, "Experimenta quibus probata nervos vagos rotatione machinae galvanomagneticae irritatos, motum cordis retardare et adeo intercipere," Omodei's Annali Universali de Medicina, Milan (3 S. 20:227, 1845).

In earlier contributions the brothers had measured the velocity of the pulse wave for the first time, in their work, "Wellenlehre," 1825, and somewhat later measured and compared the velocity of the blood and lymph corpuscles in the capillaries. This work was published in Müllers Archiv, Berlin, in 1837.

Peter Mere Latham (1789–1875), of London, a successful practitioner, was the first to emphasize the sense of impending death which at times accompanies the anginal syndrome, although Heberden had referred to a sense of anxiety. Latham's work appeared in "Lectures on subjects connected with clinical medicine: diseases of the heart," London, 1845–1846. Earlier, Latham had reported a group of cases in which sudden death did not occur in spite of the occurrence of severe seizures of angina pectoris and designated this condition as "pseudo-angina." He believed like Heberden, that the painful seizures were due to spasm of the heart.

Ernst Heinrich Weber.

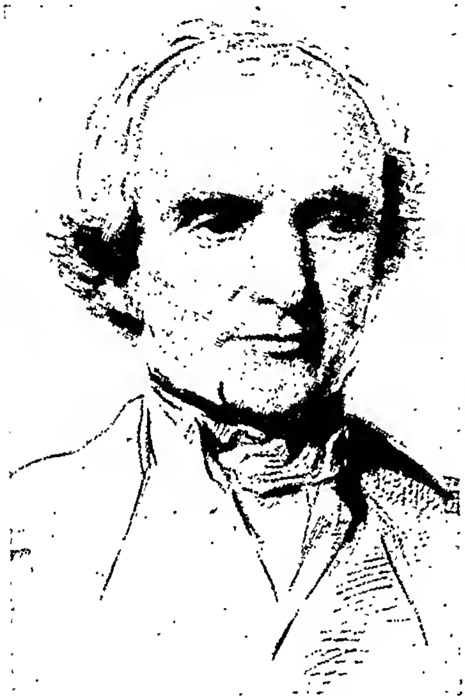
Contributions from the Irish school of medicine were again forthcoming in this period through the observations of William Stokes (1804–1878), of Dublin. The son of the regius professor of medicine at the University of Dublin, he was an Edinburgh graduate in 1825. Shortly before his graduation, Stokes published the first comprehensive work on auscultation in the English language, "An introduction to the use of the stethoscope," published in Edinburgh. He returned to Dublin after his graduation to become physician to the Dublin General Dispensary and in 1826, at the age of twenty-two years, succeeded his father as physician to the Meath Hospital. Here, with his lifelong friend, Robert Graves, he did much to improve medical teaching.

A true disciple of Laënnec, Stokes constantly attempted to broaden the field of physical diagnosis by careful observations and records together with postmortem findings. He stressed the point that in the interpretation of physical signs their identification with symptoms was of great importance.

Stokes's name is indelibly associated with two conditions that he described. He gave a lucid account of the periodic type of breathing discussed by John Cheyne in 1818, and still today this phenomenon is

known as the Cheyne-Stokes respiration. Stokes's account appeared in his book, "The diseases of the heart and the aorta," 1854. The second condition which still bears his name is heart block. Although, as previously mentioned, others, including Robert Adams (1827), had described the condition, Stokes's account especially emphasized the convulsive seizures frequently accompanying heart block. Even today, the convulsive syncopal attacks of complete heart block are known as Adams-Stokes seizures. This account of Stokes appeared in his "Observations on some cases of permanently slow pulse," 1846.

He also observed and described the phenomenon of cardiac displacement which results when a pleural effusion is rapidly absorbed. Stokes



Peter Mere Latham.

William Stokes.

called attention to the fact that the intensity of cardiac murmurs varies with changes in posture and observed that the friction rub in pericarditis can be amplified by gently increased pressure of the stethoscope and, at times, completely obliterated by heavy pressure. He observed that pericarditis at times precedes the involvement of joints in rheumatic fever and described the angina-like pains which sometimes occur in acute fibrinous pericarditis.

Stokes, contrary to prevailing opinion, correctly contended that the prognosis in mitral valvular disease was more serious than in aortic lesions. He also stressed the fact that aneurysm of the aorta does not cause enlargement of the heart. Stokes furthermore recognized and described paroxysmal tachycardia.

Carl Ludwig (1816–1895), professor of anatomy at Marburg, later professor of anatomy and physiology at Zürich, and finally professor of physiology at Leipzig, was one of the leading physiologists of this century. He was in great demand as a teacher and greatly influenced the science of physiology throughout the entire era. Ludwig taught and investigated extensively but did relatively little writing. His outstanding contribution to physiology was the introduction of the graphic method of investigation by the use of such apparatus as the kymograph, blood pump and Stromuhr. He was a pioneer in perfusion experiments on excised organs.

Carl Ludwig.

Ludwig discovered the ganglion cells in the interauricular septum in 1848. He advanced the hypothesis that lymph is formed by the diffusion of fluids from the blood through the walls of the vessels into the surrounding tissues, the hydrostatic force of this phenomenon being the capillary blood pressure. This was a collaborative study with his pupil, F. W. Noll. In his inaugural address of 1865, Ludwig discussed arterial blood pressure. He also showed that the normal beat of the animal heart is abolished by the application of faradic stimulation.

SUMMARY

The first half of the nineteenth century recorded many notable contributions dealing with the heart and circulation. The discovery most profoundly influencing the progress of cardiology was Laënnec's introduction of the stethoscope and auscultation. This, together with Corvisart's revival and augmentation of Auenbrugger's method of percussion, completed the components of modern physical diagnosis; namely, inspection, palpation, percussion and auscultation. This broadened field of diagnostic methods gave great impetus to a more precise recognition of diseases of the heart. The recognition and classification of new signs correlated with symptoms of disease and postmortem findings formed the basis for many modern concepts of heart disease, especially with reference to valvular defects. Other diagnostic achievements resulting from the new physical diagnosis were the recognition

of cardiac enlargement, the differentiation of cardiac hypertrophy from dilatation and the recognition of the various forms of pericarditis. The clinical diagnosis of thoracic aneurysm became more frequent and accurate than in previous periods.

The cardiac nerves and ganglia were discovered and the inhibitory action of the vagi on the heart was demonstrated. Physiology forged ahead rapidly with such contributions as Allan Burns's demonstration of the ischemic theory of angina pectoris and other experiments dealing with ligation of the coronary arteries. Primary experiments in the field of electrophysiology paved the way for the much later development of electrocardiography (1903), and the introduction of the graphic method of physiologic experimentation added much-needed precision in this field.

Accumulation of data regarding congenital malformations of the heart became more abundant and a concerted effort became apparent to correlate symptoms and signs attributable to these abnormalities with postmortem findings.

The causative relationship between rheumatic fever and carditis became an established fact and the concept of the occurrence of pancarditis in this disease was formulated. Bright's monumental work on the kidney and its relation to the heart and arteries opened new portals for the ultimate evolution of completely new concepts regarding the heart and circulation. Attention became focused on functional disturbances of the heart and their simulation of organic disease.

The least progress was made in the understanding of diseases of the coronary arteries. While some observers described findings which undoubtedly represented cardiac infarcts, they did so not knowing the true nature of their findings nor did they ascribe them to alterations of the coronary circulation. The significance of Burns's work was not fully appreciated until well into the twentieth century. Much difference of opinion and confusion prevailed regarding the cause and significance of angina pectoris.

Great progress occurred in medical education. This progress was largely due to the brilliance of a remarkable group of teachers dispersed in numerous schools. Baillie and Scarpa contributed extensively to the teaching of anatomy and pathology and the great physiologists, Purkinje, Matteucci, the Weber brothers and Carl Ludwig, inspired many students in their field and established the basic precepts for scientific investigation. The perfection of percussion and the discovery of auscultation created many famous clinical teachers whose chief interest dealt with diseases of the heart and lungs. Among them were the celebrated French clinicians, Corvisart, Laënnec, Cruveilhier, Bertin and Bouillaud; the famous group from the British Isles, Adams, Hodgkin, Bright, Stokes and Corrigan, and the brilliant Austrian, Skoda.

REFERENCES

Desault

Castiglioni, Arturo: A history of medicine. (Translated by E. B. Krumbhaar.) New York, Alfred A. Knopf, 1941, p. 624.
Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, p. 342.
Matas, Rudolph: Personal experiences in vascular surgery; a statistical synopsis. Ann. Surg. 112:802–839 (Nov.) 1940.

Scarpa

Castiglioni, Arturo: Op. cit., p. 601.
Garrison, F. H.: Op. cit., pp. 336–337.
Gibson, G. A.: Diseases of the heart and aorta. New York, The Macmillan Company, 1898, pp. 815 and 828.
Herrick, J. B.: A short history of cardiology. Springfield, Illinois, Charles C Thomas, 1942, p. 200.
White, P. D.: Heart disease. Ed. 3, New York, The Macmillan Company, 1944, p. 957.

Corvisart

Beeson, B. B.: Corvisart, his life and works. Ann. M. Hist. n.s. 2:297–307 (May) 1930.
Castiglioni, Arturo: Op. cit., p. 700.
°Corvisart, J.-N.: An essay on the organic diseases and lesions of the heart and great vessels from the clinical lectures of. . . . (Translated by Jacob Gates.) Philadelphia, A. Finley, 1812, 344 pp.
Garrison, F. H.: Op. cit., p. 414.
Gibson, G. A.: Op. cit., pp. 133, 322, 376, 520, 588, 624, 673, 694 and 722.
Herrick, J. B.: Op. cit., pp. 74–79 and 191.
Major, R. H.: Classic descriptions of disease; with biographical sketches of the authors. Ed. 2, Springfield, Illinois, Charles C Thomas, 1939, pp. 402–405 and 499–501.
Vierordt, Hermann: Geschichte der Herzkrankheiten. In Puschmann, Theodor: Handbuch der Geschichte der Medizin. Jena, Gustav Fischer, 1903, vol. 2, pp. 638, 639 and 642.
Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors. St. Louis, C. V. Mosby Company, 1941, pp. 277–290.

Cooper

Castiglioni, Arturo: Op. cit., p. 717.
Garrison, F. H.: Op. cit., pp. 479–480.
Matas, Rudolph: Op. cit., pp. 802–839.

Burns

°Burns, Allan: Observations on some of the most frequent and important diseases of the heart; on aneurism of the thoracic aorta; on preternatural pulsation in the epigastric region; and on the unusual origin and distribution of some of the large arteries of the human body. Edinburgh, Bryce & Co., 1809, 322 pp.
Garrison, F. H.: Op. cit., p. 486.
Gibson, G. A.: Op. cit., pp. 248, 589, 640 and 847.
Herrick, J. B.: Op. cit., p. 65.
Herrick, J. B.: Allan Burns: 1781–1813; anatomist, surgeon and cardiologist. Bull. Soc. M. Hist. Chicago. 4:457–483 (Jan.) 1935.

Vierordt, Hermann: Op. cit., p. 638.
White, P. D.: Op. cit., p. 957.
Willius, F. A.: Cardiac clinics. CXV. The historic development of knowledge relating to the coronary circulation and its diseases: the nineteenth century. Proc. Staff Meet., Mayo Clin. 21:78–79 (Feb. 20) 1946.

Wells

Bartlett, Elisha: A brief sketch of the life, character, and writings of William Charles Wells. An address delivered before the Louisville Medical Society, December 7th, 1849. Louisville, Kentucky, Prentice & Weissinger, 1849, 32 pp.
Beck, J. B.: An historical sketch of the state of American medicine before the Revolution. Ed. 2, Albany, New York, Charles van Benthuysen, 1850, 63 pp.
Castiglioni, Arturo: Op. cit., p. 706.
Garrison, F. H.: Op. cit., pp. 424 and 443.
Gibson, G. A.: Op. cit., pp. 313–314.
Herrick, J. B.: Op. cit. (A short history of cardiology), p. 153.
James, R. R.: William Charles Wells, M.D., F.R.S., 1757–1817. Brit. J. Ophth. 12: 561–569 (Nov.) 1928.
Keil, Harry: Dr. William Charles Wells and his contribution to the study of rheumatic fever. Bull. Inst. Hist. Med. 4:789–816 (Dec.) 1936.
Major, R. H.: Op. cit., pp. 227–230.
Pleadwell, F. L.: "That remarkable philosopher and physician, Wells of Charleston"; the first exponent of the theory of natural selection, discoverer of the nature of dew, and physician. Ann. M. Hist. n.s. 6:128–142 (Mar.) 1934.
Roberts, S. R.: William Charles Wells of Charleston and London. Boston M. & S. J. 193:1140–1145 (Dec. 17) 1925.
*Wells, W. C.: On rheumatism of the heart. Tr. Soc. Improved Med. Chir. Knowledge. 3:373–424, 1812.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 291–312.

John Warren

Garrison, F. H.: Op. cit., p. 499.
Herrick, J. B.: Op. cit. (A short history of cardiology), pp. 211–212.
*Warren, John: Remarks on angina pectoris. New England J. Med. & Surg. 1:1–11, 1812.
Willius, F. A.: Op. cit., p. 79.

J. C. Warren

Garrison, F. H.: Op. cit., pp. 499–500.
Herrick, J. B.: Op. cit. (A short history of cardiology), p. 212.
*Warren, J. C.: Cases of organic diseases of the heart; with dissections and some remarks intended to point out the distinctive symptoms of these diseases. M. Communicat. Mass. M. Soc. 1809–1813, Boston. 2:49–109, 1813.
Willius, F. A.: Op. cit., p. 79.

Kreysig

Gibson, G. A.: Op. cit., pp. 360 and 397.
Herrick, J. B.: Op. cit. (A short history of cardiology), pp. 81–83.

Hodgson

Benson, R. L.: General review: The present status of coronary arterial disease. Arch. Path. & Lab. Med. 2:877–878 (Dec.) 1926.
Castiglioni, Arturo: Op. cit., p. 693.
Garrison, F. H.: Op. cit., p. 424.
Herrick, J. B.: Op. cit. (A short history of cardiology), p. 216.
Willius, F. A.: Op. cit., p. 81.

Cheyne

Castiglioni, Arturo: Op. cit., p. 707.
*Cheyne, John: A case of apoplexy in which the fleshy part of the heart was converted into fat. Dublin Hosp. Rep. 2:216–223, 1818; also M. Classics. 3:705–709 (Mar.) 1939.
Garrison, F. H.: Op. cit., p. 418.
Gibson, G. A.: Op. cit., p. 645.
Herrick, J. B.: Op. cit. (A short history of cardiology), p. 118.
Major, R. H.: Op. cit., pp. 597–601.
Pettigrew, T. J.: Medical portrait gallery. Biographical memoirs of the most celebrated physicians, surgeons, etc., etc., who have contributed to the advancement of medical science. London, Fisher, Son & Co., 1840, vol. 3, 20 pp.
White, P. D.: Op. cit., p. 958.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 313–320.

Laënnec

Castiglioni, Arturo: Op cit., pp. 700–701.
Garrison, F. H.: Op. cit., pp. 411–413.
Garrison, F. H.: Laënnec. (Editorial.) Bull. New York Acad. Med. s. 2, 2:389–393 (Aug.) 1926.
Gibson, G. A.: Op. cit., pp. 48, 133, 204, 313, 651 and 654.
Herrick, J. B.: Op. cit. (A short history of cardiology), pp. 87, 88 and 91.
*Laënnec, R. T. H.: A treatise on the diseases of the chest, in which they are described according to their anatomical characters, and their diagnosis established on a new principle by means of acoustick instruments. (Translated by John Forbes.) First American Edition, Philadelphia, J. Webster, 1823, 319 pp.
Major, R. H.: Op. cit., pp. 77–79 and 405–407.
Medical Intelligence (news note): Monument to Laënnec. Boston M. & S. J. 76: 382 (June 6) 1867.
Robinson, Victor: René Théophile Hyacinthe Laënnec (1781–1826) M. Life. 28:456–469, 1921.
Vierordt, Hermann: Op. cit., pp. 638–642.
Webb, G. B.: René Théophile Hyacinthe Laënnec; a memoir. New York, Paul B. Hoeber, 1928, 146 pp.
White, P. D.: Op. cit., p. 56.
Willius, F. A.: Op. cit., p. 79.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 321–382.

Burnett

Major, R. H.: Op. cit., pp. 362–364.

Adams

*Adams, Robert: Cases of diseases of the heart, accompanied with pathological observations. Dublin Hosp. Rep. 4:353–453, 1827; also M. Classics. 3:633–696 (Feb.) 1939.
Castiglioni, Arturo: Op. cit., p. 707.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 418.
Gibson, G. A.: Op. cit., pp. 444–445, 610 and 808.
Herrick, J. B.: Op. cit. (A short history of cardiology), pp. 119 and 128–132.
Major, R. H.: Op. cit., p. 361.
Obituary: Robert Adams, M.A., M.D. Lancet. 1:145 (Jan. 23) 1875.
White, P. D.: Op. cit., p. 958.
Willius, F. A.: Op. cit., p. 82.
Willius, F. A. and Keys, T. E.: Cardiac Clinics. LXXXVIII. The influence of the Irish school of physicians. Proc. Staff Meet., Mayo Clin. 16:637–640 (Oct. 1) 1941.
Willius, F. A. and Keys, T. E.: Op. cit. (Cardiac classics), pp. 393–399.

Gintrac

Gibson, G. A.: Op. cit., pp. 229 and 306.
White, P. D.: Op. cit., p. 958.

Hodgkin

Castiglioni, Arturo: Op. cit., pp. 693 and 705.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 420 and 423.
Gibson, G. A.: Op. cit., pp. 407, 453, 473 and 487.
Major, R. H.: Op. cit., pp. 241–242 and 378–381.
White, P. D.: Op. cit., p. 958.
Willius, F. A. and Keys, T. E.: Op. cit. (Cardiac classics), p. 420.

Piorry

Castiglioni, Arturo: Op cit., p. 703.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 415
Gibson, G. A.: Op. cit., p. 136.

Larrey

Ballance, Charles: Bradshaw lecture on the surgery of the heart. Lancet. 1:1–5 (Jan. 3); 73–79 (Jan. 10); 134–139 (Jan. 17) 1920.
Castiglioni, Arturo: Op. cit., p. 714.
Chevalier, A. G.: The physicians and the medical service of the revolutionary armies. Ciba Symp. 7:250–254 (Feb.) 1946.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 487–488.
*Larrey, D. J.: Clin. Chir. 2:284, 1829; also quoted by Ballance, Charles, pp. 73–74.

Velpeau

Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 491.
King, E. S. J.: Surgery of the heart. Baltimore, Williams & Wilkins Company, 1941, p. 702.
*Velpeau, A.: Mémoir sur la piqûre ou l'acupuncture des artères dans le traitement des anévrismes. Mém. de L'Acad. des Sc. 1830; also quoted by King, E. S. J., pp. 702 and 707.

Phillips

King, E. S. J.: Op. cit., pp. 702 and 707.
*Phillips, B.: A series of experiments for the purpose of showing that arteries may be obliterated without ligation, compression or the knife. London, 1832; also quoted by King, E. S. J., pp. 702 and 707.

Mott

Castiglioni, Arturo: Op. cit., p. 721.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 501–502.

Andral

Castiglioni, Artùro: Op. cit., p. 690.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 415.
Gibson, G. A.: Op. cit., p. 329.
White, P. D.: Op. cit., p. 958.

Hope

Castiglioni, Arturo: Op. cit., pp. 693–694.
Flaxman, N.: Hope of Cardiology: James Hope, 1801–1841. Bull. Inst. Hist. Med. 6:1–21 (Jan.) 1938.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 425.
Gibson, G. A.: Op. cit., pp. 261, 299, 538, 561, 589, 724 and 850.
Herrick, J. B.: Op. cit. (A short history of cardiology), pp. 138–147.
Hope, Anne. Memoir of the late James Hope, M.D. To which are added, remarks on classical education, by Dr. Hope and letters from a senior to a junior physician, by Dr. Burder. The whole edited by Klein Grant. London, J. Churchill, 1842, 358 pp.
*Hope, James: A treatise on the diseases of the heart and great vessels, comprising a new view of the physiology of the heart's action, according to which the physical signs are explained. First American Edition, Philadelphia, Lea & Blanchard, 1842, 572 pp.
Major, R. H.: Op. cit., pp. 381–385, 409–410 and 415–416.
White, P. D.: Op. cit., p. 750.
Willius, F. A. and Keys, T. E.: Op. cit. (Cardiac classics), pp. 401–415.

Corrigan

Castiglioni, Arturo: Op. cit., pp. 693 and 707.
*Corrigan, D. J.: On permanent patency of the mouth of the aorta, or inadequacy of the aortic valves. Edinburgh M. & S. J. 37:225–245, 1832; also M. Classics. 1: 703–727 (Feb.) 1937.
Dock, George: I. Dominic John Corrigan; his place in the development of our knowledge of cardiac disease: II. The water-hammer pulse. Ann. M. Hist. n.s. 6:381–395 (Sept.) 1934.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 420 and 423.
Gibson, G. A.: Op. cit., pp. 156 and 505.
Herrick, J. B.: Op. cit. (A short history of cardiology), pp. 124–125.
Major, R. H.: Op. cit., pp. 385–390.
Obituary: Sir Dominic John Corrigan, Bart., M.D. Brit. M. J. 1:227–228 (Feb. 7) 1880.
Rolleston, Humphry: Sir Dominic Corrigan, Bart., M.D. Irish J. M. Sc. (June) 1932, pp. 261–266.
Williamson, R. T.: Sir Dominic Corrigan. Ann. M. Hist. 7:354–361, 1925.
Willius, F. A. and Keys, T. E.: Op. cit. (Cardiac classics), pp. 417–440.

Cruveilhier

Benson, R. L.: Op. cit., pp. 876 and 878.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 445–446.
Herrick, J. B.: Op. cit. (A short history of cardiology), pp. 222–224.
Major, R. H.: Op. cit., pp. 687–688.
Willius, F. A.: Op. cit., p. 82.

Bertin

Gibson, G. A.: Op. cit., pp. 640, 694 and 721.
Major, R. H.: Op. cit., pp 407–409.
Vierordt, Hermann: Op. cit., pp. 638–639.
Willius, F. A. and Keys, T. E.: (Cardiac classics), p. 443.

Lobstein

Castiglioni, Arturo: Op. cit., pp. 691–692.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 843 and 846.
White, P. D.: Op. cit., p. 958.

Bouillaud

*Bouillaud, J.-B.: Traité clinique des maladies du coeur. Paris. J.-B. Baillière, 1835, vol. 2, pp. 170–192.
Castiglioni, Arturo: Op. cit., p. 700.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 413–414.
Gibson, G. A.: Op. cit., pp. 148, 284, 390, 673 and 736.
Herrick, J. B.: Op. cit. (A short history of cardiology), pp. 147–151.
Lereboullet, P.: J. Bouillaud (1796–1881). Paris méd. 16:177–183, 1914.
Major, R. H.: Op. cit., pp. 230–233.
Rolleston, J. D.: Jean Baptiste Bouillaud (1796–1881). A pioneer in cardiology and neurology. Proc. Roy. Soc. Med. (Section of the history of medicine.) 24 (pt. 2):1253–1262 (Apr. 15) 1931.
Willius, F. A. and Keys, T. E.: Op. cit. (Cardiac classics), pp. 441–455.

C. J. B. Williams

Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 630.
Gibson, G. A.: Op. cit., pp. 62, 319, 320 and 802.
White, P. D.: Op. cit., p. 615.

Bright

*Bright, Richard: Reports of medical cases selected with a view of illustrating the symptoms and cure of diseases by a reference to morbid anatomy. London, Longman, 1827, vol. 1, 231 pp.
Castiglioni, Arturo: Op. cit., pp. 703–705.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 420–422.
Gibson, G. A.: Op. cit., pp. 398 and 729.
Major, R. H.: Op. cit., pp. 580–588.
Vierordt, Hermann: Op. cit., p. 642.
White, P. D.: Op. cit., p. 958.

John C. Williams

White, P. D.: Op. cit., pp. 4–6.

Skoda

Castiglioni, Arturo: Op. cit., p. 711.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 431–432.
Gibson, G. H.: Op. cit., pp. 124 and 136.
Herrick, J. B.: Op. cit. (A short history of cardiology), p. 96.
Major, R. H.: Op. cit., pp. 609–612.
Vierordt, Hermann: Op. cit., pp. 640, 644 and 646.
White, P. D.: Op. cit., p. 958.

Purkinje

Castiglioni, Arturo: Op. cit., p. 679.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 459–461.
White, P. D.: Op. cit., p. 958.

Hall

Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 470–471.
Herrick, J. B.: Op. cit. (A short history of cardiology), pp. 218–219.
White, P. D.: Op. cit., p. 958.
Willius, F. A.: Op. cit., p. 82.

Erichsen

Gibson, G. A.: Op. cit., pp. 68 and 626.
Gross, Louis: The blood supply to the heart; in its anatomical and clinical aspects. New York, Paul B. Hoeber, 1921, p. 79.
Herrick, J. B.: Op. cit. (A short history of cardiology), p. 219.
Willius, F. A.: Op. cit., p. 86.

Chevers

Gibson, G. A.: Op. cit., pp. 475, 568 and 640.
Herrick, J. B.: Op. cit. (A short history of cardiology), p. 190.
White, P. D.: Op. cit., pp. 657–658.

Fauvel

Gibson, G. A.: Op. cit., pp. 157, 158 and 520.
Major, R. H.: Op. cit., pp. 410–412.
Vierordt, Hermann: Op. cit., p. 640.

Matteucci

Castiglioni, Arturo: Op. cit., p. 689.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 462 and 534.
White, P. D.: Op. cit., p. 171.
Willius, F. A. and Keys, T. E.: Op. cit. (Cardiac classics), pp. 717–721.

Forbes

Allbutt, Clifford: Diseases of the arteries including angina pectoris. London, Macmillan and Co., Limited, 1915, vol. 2, p. 224.
Willius, F. A.: Op. cit., pp. 79–80.

Weber and Weber

Castiglioni, Arturo: Op. cit., pp. 685 and 781.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 468–470.
White, P. D.: Op. cit., p. 958.

Latham

Gibson, G. A.: Op. cit., pp. 248, 762 and 775.
Herrick, J. B.: Op. cit. (A short history of cardiology), p. 133.
Hirschfelder, A. D.: Diseases of the heart and aorta. Ed. 3, Philadelphia, J. B. Lippincott Company, 1918, 732 pp.
Willius, F. A.: Op. cit., p. 80.

Stokes

Castiglioni, Arturo: Op. cit., pp. 693 and 707.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 419.
Gibson, G. A.: Op. cit., pp. 164, 317, 329, 331, 503, 727, 808 and 846.
Herrick, J. B.: Op. cit. (A short history of cardiology), pp. 115–117.
Major, R. H.: Op. cit., pp. 431–432.
Stokes, William: William Stokes, his life and work (1804–1878); by his son William Stokes. London, T. F. Unwin, 1898, 256 pp.
°Stokes, William: Observations on some cases of permanently slow pulse. Dublin Quart. J. M. Sc. 2:73–85, 1846; also M. Classics. 3:727–738, 1939.

*Stokes, William: Fatty degeneration of the heart. In: The diseases of the heart and aorta. Dublin, Hodges & Smith, 1854, pp. 320–327; also M. Classics, 3:739–746, 1939.
Willius, F. A. and Keys, T. E.: Op. cit. (Cardiac classics), pp. 457–469 and 483–489.

Ludwig

Castiglioni, Arturo: Op. cit., p. 781.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 555–556.
White, P. D.: Op. cit., p. 958.

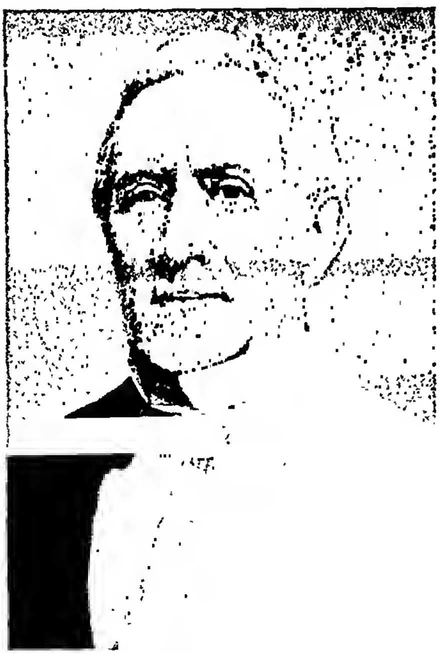
* Indicates original source consulted by the authors.

7

THE SECOND HALF OF THE NINETEENTH CENTURY

*All knowledge attains its ethical value and its human significance only by the humane sense in which it is employed. Only a good man can be a great physician.**

THE SECOND half of the nineteenth century witnessed the rapid advance of German and Austrian medicine. Berlin, Leipzig, Vienna and other centers, with their large hospitals and clinics and abundant clinical material, attracted physicians from all corners of the world. Excellent teaching facilities and outstanding teachers together with extensive and well-organized postmortem material largely accounted for the shift from France to Germany and Austria. The medicine of the British Isles also surged ahead although it was second in prestige to the aforementioned continental clinics. American medicine was making progress but was still in the stage of adolescence. During the closing years of the century the education of the American physician was not considered complete until he had spent some time abroad. It was not until well into the twentieth century that American medicine came of age.



Sir Richard Quain.

While the relationship of coronary disease to specific symptoms and the effects of sudden closure of a coronary artery on the heart still remained obscure and confused, continued interest in this problem was manifest and an increasing number of clinical reports with postmortem findings appeared in the literature. Even though a clear interpretation of cause and effect was lacking, various observers contributed data which later, when viewed in retrospect, aided materially in the clarification of this vexing problem.

The illustrious Englishman, Sir Richard Quain (1816–1889), of London, made important observations on this subject but did not fully

* Hermann Nothnagel (1841–1905), quoted by Garrison, p. 16.

or correctly interpret his findings. In 1850, he published a comprehensive review, "On fatty diseases of the heart," in which he described myocardial changes which correspond to our present-day concepts of anemic infarcts. Quain referred to them as "fatty degeneration." He contended that the designated "fatty changes" were the result of both constitutional causes and local nutritional disturbances. In supplementing the statement concerning local nutritional causes, Quain stated that he had observed cases in which the myocardial changes were localized and corresponded to the region supplied by a coronary artery which was extensively "ossified." It is thus apparent that Quain was remarkably close to comprehending the present-day concept of infarct production.

Like others of this era, Quain believed the coronary arteries to be end arteries. He regarded the arcus senilis as indicative of fatty myo-

Claude Bernard and students.

cardial changes but did not understand its relation to atherosclerosis. He reported on 100 cases of cardiac rupture and called attention to the fact that death occurred instantaneously in seventy-one while in the remaining cases, dissolution occurred over a period of several hours. Quain also called attention to the frequency of cardiac hypertrophy in patients dying of apoplexy but he did not have the advantage of recording blood pressure and therefore did not conceive the relationship of hypertension to cardiac hypertrophy and cerebrovascular accidents.

The first half of the nineteenth century had witnessed considerable progress in the province of physiology. Remarkable advances occurred in the ensuing period and many distinguished physiologists participated in this progress. Among them was Claude Bernard (1813–1878), of

Paris, a student of the celebrated Magendie and ultimately his successor. In his youth, Bernard had aspirations to become a dramatic poet after successfully completing two works, "La Rose du Rhône," a vaudeville comedy, and "Arthur de Bretagne," a five-act tragedy. He was, however, dissuaded from making literature and poetry his career and finally decided to study medicine. Magendie's influence and inspiration guided Bernard's interest into the field of physiology. He is designated as the greatest physiologist of modern France and the founder of experimental medicine.

While most of Bernard's splendid investigations were concerned with the physiology of digestion and of the central nervous system he also made significant contributions relating to the vascular system. By means of ingenious experiments he demonstrated the vasomotor nerves and their mechanism. Bernard sectioned the sympathetic nerve of a rabbit and observed an increase of the local temperature of the ear where a decrease of temperature had been anticipated. A markedly increased vascularity of the ear also occurred. Uncertainty existed whether the congestion in the vessels of the rabbit's ear accounted for the rise of temperature. The experiment was then repeated after two of the veins to the ear had been ligated and the same results were obtained. These observations led Bernard to conclude that the sympathetic nerves control temperature. This work appeared in 1854.


William Senhouse Kirkes.

Shortly thereafter, Bernard continued his experiments and demonstrated that the sympathetics are the nerves of vasoconstriction and the chorda tympani is the nerve of vasodilatation.

One of the earliest and most concise accounts of the disease now known as "bacterial endocarditis" was recorded by William Senhouse Kirkes (1823–1864), of London. A brilliant student whose career was terminated at the early age of forty-one years, he obtained his early medical training at St. Bartholomew's Hospital and completed his training at the University of Berlin, from which institution he received the degree of Doctor of Medicine in 1846. Two years later Kirkes was appointed medical registrar and demonstrator of morbid anatomy at St. Bartholomew's Hospital. In 1850 he became a licentiate of the

Royal College of Physicians and successively became assistant physician and physician to the aforementioned hospital.

Kirkes's classic article, "On some of the principal effects resulting from the detachment of fibrinous deposits from the interior of the heart, and their mixture with the circulating blood," was published in 1852. He discussed the detachments from vegetations on the valves and mural endocardium and how they are conveyed by the blood stream, according to their location in the right or the left side of the heart, to remote parts of the body and abruptly obstruct large arteries. Kirkes also concerned himself with the detachment and dissemination of minute particles which produce typhoidal and phlebitic symptoms.

A classic physiologic experiment still known by the investigator's name was performed by Hermann Stannius (1808–1883), of Hamburg. He applied a ligature at the junction of the auricle and the sinus venosus of the frog's heart which resulted in standstill of the heart. The application of a second ligature to the auriculoventricular groove caused the ventricles to beat again. In this experiment, Stannius demonstrated the important fact that the ventricles are endowed with the property of initiating their own rhythm in heart block (idioventricular rhythm). This work appeared in Müllers Archiv in 1852.

Paul Broca.

The first to recognize the potential dangers of arteriovenous fistula and to approach the condition from the surgical standpoint was Paul Broca (1824–1880), of Paris. Particularly known for his contributions to neurology and neurosurgery, he was surgeon at St. Antoine, La Pitié, the Hôpital des Cliniques and Hôpital Necker.

Matas in his comments on the development of the surgical treatment of arteriovenous fistula stated:

> As far as the arteriovenous aneurysms are concerned, the old teaching regarded them as relatively benign and not liable to rupture—a tradition which lingered from the days of William Hunter (1774); they were allowed to remain undisturbed except by purely mechanical methods of compression. When complicated by large varicose sacs, by infection or by other disabling varicosities they were attacked by the open method, only as a last resort. When surgery was required, the proximal artery was ligated, but, as experience too frequently proved, with no cure and often gangrene of the limb. It was only after the great treatises of Paul

Broca, in the fifties, and Pierre Delbet and von Bramman, in the eighties, that the principles underlying the cure of arteriovenous aneurysms were clearly understood and that the extirpation of the fistulous segments or the quadruple ligature were more frequently resorted to.

A pioneer in the study of blood pressure was Karl von Vierordt (1818–1884), the able professor at the University of Tübingen. In 1855, twenty-one years before Marey's contributions, he had studied the blood pressure in human subjects by determining the weight required to obliterate the radial pulse. This method, however, was very inaccurate. Vierordt was the first to make accurate erythrocyte counts, described the first sphygmograph (1855) and invented a hemotachometer in 1858 in order to record the velocity of blood flow.


Friedrich Wilhelm Bidder.

One of Germany's leading physiologists of this era was Friedrich Wilhelm Bidder (1810–1894). In 1852 he discovered the ganglion cells located at the auriculoventricular junction. Bidder also investigated the sympathetic nervous system and in 1852, in collaboration with Schmidt, disproved the belief of Claude Bernard and Barreswil, Lehmann and others that the free acid contained in gastric secretion is lactic acid.

The originator of the injection-corrosion method of preparing and studying the vascularity of organs and structures was Josef Hyrtl (1810–1894), of Vienna. He was assistant to the celebrated Czermak at Vienna, became prosector in anatomy in 1833 and three years later, at the age of twenty-six years, was appointed professor of anatomy at the University of Prague. In 1844, Hyrtl was called to the chair of anatomy at Vienna and served in this capacity for thirty years. A brilliant lecturer, he attracted great audiences, and spoke and wrote equally well in German and in Latin. Hyrtl is credited as the founder of topographic anatomy and his famous "Lehrbuch," first published in 1846, passed through twenty-two editions and was translated into many languages. Its popularity rested on its authenticity and remarkably clear presentation, for it was unaccompanied by illustrations until the twentieth edition appeared.

Hyrtl was possessed of unusual originality and imagination and these characteristics were personified in his work, "Die Corrosions-Anatomie

und ihre Ergebnisse," which appeared in 1873. He studied the vascularity of the heart and other organs by injecting a metallic alloy of low melting point into the vessels and, after the substance hardened, subjected the organ to corrosion in strong acid. Nothing remained but the metallic cast of the vessels. With regard to the heart, Hyrtl concluded that this method failed to demonstrate anastomoses between coronary arteries. This conclusion was not universally accepted and subsequent workers have shown that Hyrtl's failure to demonstrate anastomoses was due to the technical limitations of his method.

He discovered the portal vein of the suprarenal capsule, as well as the branchial veins in fishes, and described the origin of the coronary arteries (1854). After Hyrtl's retirement from active teaching in 1874 he produced three classic works on Hebraic and Arábic elements in anatomy, "Das Arabische und Hebraische in der Anatomie," Vienna, 1879; a work on anatomic terminology, "Onomatologia anatomica," Vienna, 1880; and one on ancient German anatomic expressions, "Die alten deutschen Kunstworte der Anatomie," Vienna, 1884.


Josef Hyrtl.

One of the greatest pathologists of all times was Rudolph Ludwig Karl Virchow (1821–1902), of Berlin, a student of the famous Johannes Müller, who had inspired him to pursue the study of morbid anatomy. Virchow graduated from the University of Berlin in 1843. Two years later he became Froriep's prosector at the Charité, full prosector in 1846 and, in 1847, founded the "Archiv für pathologische Anatomie und Physiologie und für klinische Medizin," which became known throughout the world as "Virchows Archiv."

In 1848 Virchow was commissioned by the Prussian Government to investigate the epidemic of typhus which was raging among the weavers of Upper Silesia. He found deplorable conditions among the workers, poor hygiene, bad working conditions, poverty and undernourishment, and his report was so frank and critical, demanding charity and care for the unfortunates, that the authorities not only refused to acknowledge his recommendations but also deprived him of his prosectorship. Virchow's report was interpreted as suggesting democracy in place of the existing Imperial Government. At this point, his friend Scanzoni,

the celebrated obstetrician, intervened and secured for Virchow the professorship of pathologic anatomy at the University of Würzburg. After spending seven years at this post he was invited, under honorable terms, to accept the chair of pathologic anatomy at the University of Berlin. He was installed in 1856 and at the same time also assumed the directorship of the Pathological Institute.

Virchow's researches and writings covered virtually every phase of pathologic anatomy. His most notable work in the province of cardiovascular disease was his researches concerning thrombosis and embolism (1846–1856). He demonstrated the embolic nature of the pulmonary lesions in bacterial (malignant) endocarditis. He showed that the thrombus in a vein is the primary product of phlebitis and that detached portions of the thrombus are transported to the lungs by way of the venous circulation. Virchow proved this point by removing a large embolus which completely obstructed a pulmonary artery and by showing that it fitted perfectly to the surface of the primary thrombus in the peripheral vein.

Rudolf Ludwig Karl Virchow.

He believed that an abnormal narrowness of the entire aorta occurred in patients who had chlorosis. Virchow was the first to describe and name endarteritis. In his investigations of the myocardium he recognized two forms of inflammatory changes which he classified as parenchymatous and interstitial. He failed, however, to recognize the true significance of the fibrous myocardial changes of chronic myocardial ischemia and referred to them as indicating chronic myocarditis. This was unfortunate, because Virchow's brilliance and great reputation made it almost impossible for lesser lights to disagree with the master and thus for many succeeding years the concept of myofibrosis and myocardial infarction was not fully conceived or appreciated. Even well into the twentieth century, chronic myocarditis haunted the medical profession and served as a convenient category for uncertain diagnoses.

One of Virchow's greatest contributions to pathology was the introduction of the cellular concept of morbid anatomy. This famous work, which completely revolutionized this science, appeared in 1858 under

the title of "Die Cellular-pathologie in ihrer Begründung auf physiologische und pathologische Gewebelehre."

An important experiment in electrophysiology which virtually established the basis of electrocardiography was contributed by Albert von Kölliker (1817–1905), of Zurich and Würzburg. He graduated from the University of Heidelberg in 1842. During his student days he had attended some of Johannes Müller's lectures in Berlin. Kölliker became prosector to the celebrated Henle at Zurich and from this great teacher learned the basis of histology, in which field he ultimately excelled his master. Kölliker was appointed professor of anatomy at Zurich in 1846 and a year later accepted the same post at the University of Würzburg, where he remained throughout the rest of his active life.

Albert von Kölliker.

He applied Matteucci's galvanic frog experiment to the heart and, in collaboration with H. Müller, published his important work on the action currents of the heart. In these experiments it was demonstrated that with each beat of the frog's heart a definite electric current was produced. The article recording this work appeared in 1855 and was titled, "Nachweis der negativen Schwankung am natürlich sich kontrahierenden Muskel." This important observation is the basis of electrocardiography.

Kölliker also rediscovered the branched muscle layers in the heart which van Leeuwenhoek had observed approximately two hundred years earlier.

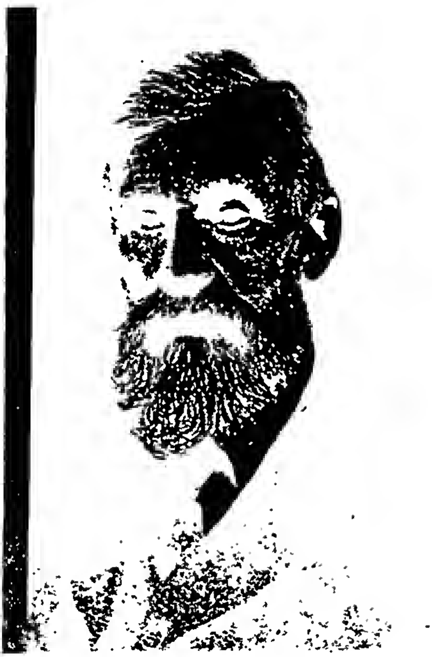
An important discovery concerned with the physiology of the heart was that of Sir Michael Foster (1836–1907). A pupil of the celebrated William Sharpey (1802–1880), Foster was appointed professor of physiology at Cambridge in 1883 and became one of the greatest teachers of his time. Among his students were many distinguished teachers and investigators who represented virtually all branches of biology. Among them were Francis Maitland Balfour in embryology, Archibald Liversidge in chemistry, Milnes Marshall in zoology, Sidgwick in animal morphology, Ray in pathology, Francis Darwin in vegetable morphology and Vines in experimental botany.

In 1859, working with the heart of the snail, Foster demonstrated

that any part of the heart separated from the rest will beat rhythmically. He also showed that the heart destitute of its ganglia continues to beat in a perfectly normal manner. From these findings, Foster concluded that rhythmicity is a specific and inherent quality of the heart muscle in general and not of any one localized portion or of its innervation.

In collaboration with Balfour, he published an important work, "Elements of embryology," in 1874 and two years later with J. N. Langley published a book on practical physiology. Also in 1876, Foster published his famous "Textbook of physiology," of which seven editions appeared and which was translated into German, Italian and Russian.

Probably the earliest reference in the literature definitely correlating cardiac infarction with coronary thrombosis is the account of the famous Swedish physician, Pehr Henrik Malmsten (1811–1883), who also discovered Balantidium coli and Trichophyton tonsurans. In 1861, he reported a case of spontaneous rupture of the left ventricle. Benson quotes him as follows:



Sir Michael Foster.

> Microscopically, the muscle fibers were here destroyed and replaced by a highly granular detritus, mingled here and there with fatty granules. In places there were small areas visible even to the naked eye, where only connective tissue remained, buried in the degenerated mass. . . . The clot in the coronary artery was undoubtedly old. The arterial obstruction had resulted in a slow softening of the muscular tissue. Finally rupture appears to have occurred slowly.

Interesting and important contributions were made by the great French clinician, Paul-Louis Duroziez (1826–1897). A graduate of the Faculté de Médecine of Paris, he was a student of the celebrated Bouillaud, who kindled the young man's interest in diseases of the heart. While still engaged in the undergraduate study of medicine in 1850, Duroziez was awarded the Corvisart Prize for his excellent clinical study on "Therapeutic properties and physiologic action of digitalis." He received the degree of Doctor of Medicine in 1851 and his graduation thesis was titled: "Clinique de la Charité, Service de M. le Professeur Bouillaud, Sémestre d'Hiver 1850–1851."

In 1856, Duroziez was appointed chief of a clinic at La Charité in Bouillaud's service, where he remained until 1858. In 1867 he was appointed physician of the Bureau of Welfare of the First Ward of Paris

and in 1879 he became a member of the Commission of Public Hygiene and Health of the First Ward. He was awarded the Itard Prize of the Académie de Médecine for his splendid work, "Traité clinique des maladies du coeur," in 1891 and also the Montyon Prize of the Institut de France in the same year.

Indicating his profound interest in diseases of the heart, Duroziez once remarked to a friend, "As long as my own heart beats, I shall continue to auscultate the hearts of others." He used a unique metaphor in his differentiation of the right and the left chambers of the heart. He considered the heart as a separate being endowed with a male half, the left ventricle, and a female half, the right ventricle. The former, he thought, was calm, regular and stable; the latter, he considered, was nervous, impressionable and often disordered. In his original work on the duality of the heart, "De la dualité du coeur," 1893, Duroziez referred to the four chambers of the heart as four horses fastened to the same chariot. He stated that this arrangement permitted a ready break in equilibrium resulting in poorly co-ordinated movement.

Probably his most outstanding contribution was the description of the double murmur heard in the femoral artery in aortic insufficiency, which still today is known as "Duroziez's sign." This publication appeared as "Du double souffle intermittent crural, comme signe de l'insuffissance aortique" in 1861.

Duroziez also described the pure form of mitral stenosis so accurately that for some time this lesion was referred to as "Duroziez's disease." His description of this lesion and its signs appeared in the article, "Du rétrécissement mitral pur," 1877. He also called attention to his detection of a large patency of the foramen ovale in an adult in the complete absence of physical signs.

Duroziez was one of the first to call attention to the development of delirium during the administration of digitalis, 1874.

In his teaching, Duroziez introduced the onomatopoetic "fout-tatarou" to describe the various abnormal sounds heard in mitral stenosis. He also called attention to certain sequelae of mitral stenosis, such as embolism, aphasia and hemiplegia, and noted the predominance of mitral disease among females.

An American pioneer in the use of auscultation was Austin Flint (1812–1886), who was born in Petersham, Massachusetts. A graduate of Harvard Medical School in 1833, he was a student of Jacob Bigelow (1787–1879) and James Jackson (1777–1868). After spending three years in private practice at Northampton and Boston he moved to Buffalo, New York, and in 1844 was appointed professor of the theory and practice of medicine at Rush Medical College in Chicago. He held this position for only one year and then returned to Buffalo, where he established the Buffalo Medical and Surgical Journal and held the editorship of this publication for ten years.

In 1847, together with Drs. James P. White and Frank H. Hamilton, Flint founded the Buffalo Medical College, which is now the School of Medicine of the University of Buffalo. In 1852 he accepted the chair of the theory and practice of medicine at the University of Louisville but held this position only four years. Flint then returned to Buffalo to become professor of pathology and clinical medicine. He spent the winters from 1858 to 1861 in New Orleans, where he filled the post of professor of clinical medicine at the New Orleans School of Medicine and was attending physician at Charity Hospital.

Flint was one of the first to use the binaural stethoscope. His classic account was based on the finding disclosed in the case of a patient whom he examined at Charity Hospital. The patient presented the typical signs of aortic insufficiency and stenosis but in addition to these signs, a presystolic murmur was audible at the apex of the heart. However, at postmortem examination, the mitral valves were found to be normal. This account was published three years later (1862) under the title "On cardiac murmurs." Since that time, the murmur described by Flint has been known by his name.

Austin Flint.

Flint was a prolific writer and contributed other important articles. In 1881 he addressed the International Medical Congress in London on "The analytical study of auscultation and percussion with reference to the distinctive characteristics of the pulmonary signs." Neither Laënnec nor his followers with the exception of Skoda paid any attention to changes in the pitch of percussion notes or respiratory sounds and credit for this emphasis belongs to Austin Flint. This work appeared in an essay, "The variations of pitch in percussion and respiratory sounds and their application to physical diagnosis," for which he received the annual prize of the American Medical Association in 1852.

In 1859 he published his book, "A practical treatise on the diagnosis, pathology and treatment of diseases of the heart."

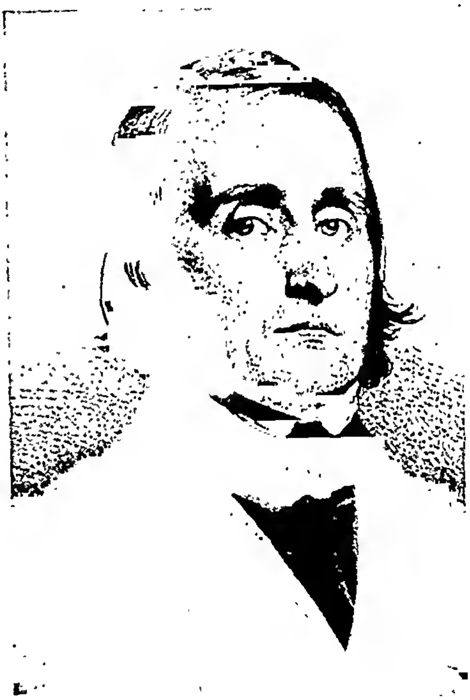
Flint disapproved of the custom of associating any physical sign with the name of the discoverer and stated: "So long as signs are determined from fancied analogies, and named from these or after the person who describes them, there cannot but be obscurity and confusion."

He died suddenly from a cerebral hemorrhage at the age of seventy-three.

A pioneer in advocating open incision of the pericardium for effusion was Armand Trousseau (1801–1867), of Tours and Paris. He was professor of the Paris Faculty and physician to the Hôpital St. Antoine and Hôtel Dieu. Most of Trousseau's writings were incorporated in his volume, "Clinique médicale de l'Hôtel Dieu," 1861.

He described the symptoms and signs of pericardial effusion. The following quotation appeared in Ballance's article (see References)·

> There is great oppression of the breathing and the facial anxiety increases from day to day. The pericardial dullness soon covers a wide area. It extends from beyond the right edge of the diaphragm. The precordial region is arched. The pulsations of the heart become obscure and muffled as if distant and finally cease to be heard. The pulse is small and rapid. At the end of a few weeks the dyspnea is extreme. The patient cannot lie down, the lips are blue, the skin cold and livid, the extremities oedematous, and the face puffy. There is no albuminuria.



Armand Trousseau.

Trousseau was the first in Paris to perform tracheotomy (1831). He wrote a classic description of tuberculosis laryngitis in 1837, was a pioneer in the use of thoracentesis (1843) and employed intubation in 1851.

An interesting and important study concerned with the coronary circulation was made by the Dane, Peter Ludwig Panum (1820–1885). He was an assistant to Claude Bernard and later taught physiology at the universities of Kiel and Copenhagen. Panum confirmed Erichsen's experiments but instead of ligating the coronary arteries he utilized the method of experimental emboli. While death of the animals occurred, the cessation of cardiac action was gradual rather than abrupt. These experiments were reported in his article, "Experimentelle Beiträge zur Lehre von der Embolie" in Virchows Archiv, 1862.

While still an intern, in 1846, Panum conducted a classic epidemiologic study. A severe epidemic of measles occurred in the Faeroes, the inhabitants of which had not been exposed to the disease for sixty-five years. Six thousand of the 8,000 inhabitants were stricken and Panum was able to establish the period of contagion, the time of appearance of the rash, the differentiation of measles from cowpox and smallpox and the immunity conferred by a single attack.

A classic account of an intermittent disturbance of the peripheral vascular system was recorded by Maurice A.-G. Raynaud (1834–1881), of Paris. He was the son of a prominent university professor and Raynaud's uncle was the eminent surgeon, Vernois. A Paris graduate, Raynaud received the degree of Doctor of Medicine in 1862.

In 1862 his famous article "De l'asphyxie locale et de la gangrène symétrique des extrémités" was published. Raynaud described the episodes of discoloration of the skin of the fingers and toes which occurred particularly on exposure to cold. He believed these phenomena to result from increased sensitivity of the sympathetic nervous system. He contended that these manifestations could eventuate in gangrene of the fingers or toes without occlusion of the arteries or veins. These symptoms are still today known as "Raynaud's phenomena." Regrettably, many of the cases cited by Raynaud did not represent bona fide examples of the disease.


Maurice Raynaud.

Seventeen years later (1879) Raynaud utilized the same subject for his inaugural thesis for the Academy of Medicine. In 1862 he wrote a book dealing with the status of medicine and medical education during the time of the celebrated dramatist Molière (1622–1673).

Raynaud suffered from heart disease for many years and died as the result of this infirmity at the early age of forty-seven years.

An interesting but erroneous concept regarding the cause of angina pectoris was advanced by the celebrated clinician, Étienne Lancereaux (1829–1910), of Paris. He studied the cardiac plexus, reported the finding of lesions in this structure and advanced the belief that neuritis of these nerve tissues was responsible for the painful seizures. This hypothesis received some acceptance, for its presentation came at a time when much confusion prevailed regarding the true nature of angina pectoris. This work was published in an article, "De l'altération de l'aorte et du plexus cardiaque dans l'angine de poitrine," in 1864.

Lancereaux also described gummata of the pericardium without other cardiac involvement in syphilis of the lung. He discussed chronic myocarditis and stated that it occurred from toxic causes as well as being associated with endocarditis and pericarditis. With Philippe Ricord

(1799–1889), Lancereaux described syphilitic cirrhosis of the liver. Ricord had named the three stages of syphilis. Lancereaux also associated diabetes mellitus with disease of the pancreas.

A new method of treating aneurysms, including those of the abdominal aorta, was introduced by Charles Hewitt Moore (1821–1870) and Charles Murchison (1830–1879), of London, in 1864. With the intention of producing mural thrombosis and ultimate organization of the thrombus within the sac of the aneurysm, they passed fine wire into the sac and allowed it to remain there. The description of this work appeared in their article, "On a new method of procuring consolidation of fibrin in certain incurable aneurisms." This method, as history reveals, did not prove to be effective.

The most complete volume up to this time dealing with congenital malformations of the heart was compiled by Thomas Bevill Peacock (1812–1882), of London. The usual congenital anomalies were included together with extremely rare combinations of defects. It was the most comprehensive work published prior to Maude E. Abbott's "Atlas," published in 1936. Peacock's book, "Malformations of the human heart," London, appeared in 1866.

Étienne Lancereaux.

Peacock favored the belief that cyanosis in congenital heart disease resulted from venous stasis rather than from the admixture of venous and arterial blood. In 1874 he published a report on a dissecting aneurysm of the aorta which was discovered at postmortem examination. The patient was a sixty-one-year-old actor whose death occurred suddenly following a severe but brief episode of precordial pain.

The most important therapeutic contribution to cardiology since Withering's introduction of digitalis in 1785 was that of Sir Thomas Lauder Brunton (1844–1916), of Edinburgh and London (see special biography). He was a graduate of the University of Edinburgh, receiving the degree of Bachelor of Medicine in 1866 and the degrees of Master of Surgery and of Bachelor of Science in 1867. In 1868, after winning the gold medal award for his thesis, "Digitalis with some observations on the urine," he received his Doctorate in Medicine.

Brunton then pursued graduate study on the continent at various

medical centers in Germany, Austria and Holland. Among his teachers were Ernst Wilhelm von Brücke, Isidor Rosenthal, Ludwig Traube, Willy Kühne and Carl Ludwig. He received his greatest inspiration while working with Carl Ludwig at Leipzig and here did his first work on the independent contraction of the arterioles and capillaries. In this experimental work, Brunton made observations on the effect of amyl nitrite and sodium nitrite on the smaller vessels which undoubtedly created the basic concept for a subsequent important contribution.

His classic article, "On the use of nitrite of amyl in angina pectoris," was published in 1867. In this work he described the prompt relief usually resulting from the inhalation of amyl nitrite in angina pectoris. The following quotation from Brunton's article is of interest: "As I believed the relief produced by the bleeding to be due to the diminution it occasioned in the arterial tension, it occurred to me that a substance which possesses the power of lessening it in such an eminent degree as nitrite of amyl would probably produce the same effect and might be repeated as often as necessary without detriment to the patient's health."


Thomas Bevill Peacock.

In considering cardiac pain in general, Brunton was of the opinion that it was the result of weakness of the heart and occurred in proportion to the resistance which the organ was required to overcome. He ascribed angina pectoris specifically to vascular spasm of the vessels of the heart.

Brunton received knighthood in 1900 and was created a baronet in 1908.

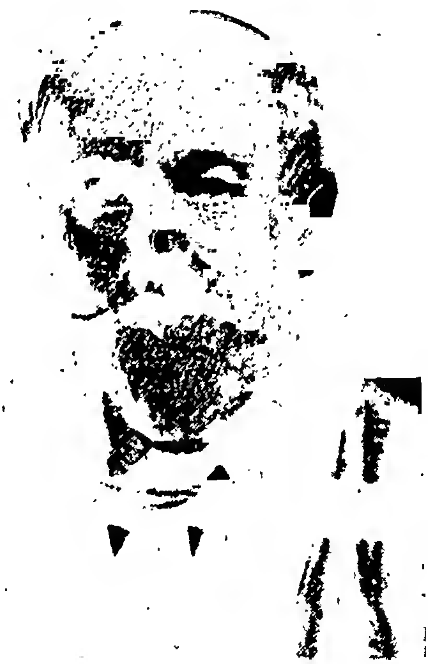
One of the earlier accounts of paroxysmal tachycardia was recorded by Richard Payne Cotton (1820–1877), a successful practitioner of London. William Stokes had reported a case thirteen years earlier, in 1854. Cotton received his medical education at St. George's Hospital and had engaged in graduate study at Paris. He was on the staff of the Hospital for Consumption and Diseases of the Chest at Brompton for many years and retired from this post in 1875.

Cotton's article, "Notes and observations upon a case of unusually rapid action of the heart (232 per minute)," appeared in 1867. In the treatment of this patient he administered antacids, stimulants of vari-

ous kinds and aperients without arresting the paroxysm but made the comment that during this treatment segments of tapeworm were expelled. Later, digitalis in conservative doses was administered and during this period of the treatment, the attack suddenly became arrested.

The originator of a new hypothesis regarding the cause of angina pectoris was the brilliant German clinician, Hermann Nothnagel (1841–1905). He was a student of the celebrated Traube and Virchow and was von Leyden's assistant at Königsberg from 1865 to 1868. Nothnagel later became professor of medicine at Freiburg in 1872, at Jena in 1874 and Vienna in 1882. He held the latter post for twenty-three years.

Nothnagel introduced a hypothesis regarding the cause of angina pectoris, which for a time was quite widely acclaimed. He introduced the term "stenocardia" and contended that the symptoms of angina pectoris did not arise from primary disease of the heart but rather from secondary factors comprising generalized arterial spasm. Thus, the vasomotor hypothesis of angina pectoris came into being. This work appeared in his article, "Angina pectoris vasomotoria," 1867.


Richard Payne Cotton.

Nothnagel also ascribed pain to valvular lesions and reported on the relative frequency of this symptom according to the valve or valves involved. He further suggested that paroxysmal tachycardia resulted from irritation of the sympathetic nervous system.

Nothnagel's most memorable work, of which he was editor, was the twenty-four volume "Handbuch der speziellen Pathologie und Therapie," which appeared between 1894 and 1905. Afflicted with angina pectoris, Nothnagel presented his own symptoms in writing shortly before his death in 1905. A photostatic copy of this one page of notes was reproduced in a short explanatory article and is of particular historic interest because it apparently represents his last recorded medical writing.

An outstanding French clinician of this period who contributed extensively to the knowledge of the heart was Pierre-Carl-Édouard Potain (1825–1901), of Paris. He received the degree of Doctor of Medicine from the University of Paris in 1853 and while still a student

served for a time at the famous Hôpital Salpêtrière where he was stricken with cholera. In 1856 he became assistant to Jean-Baptiste Bouillaud (1796–1881) and later became chief of Bouillaud's clinic. He also served on the staffs of the Hôpital St. Antoine and the Hôpital Necker (the hospital where Laënnec worked from 1816 until his death in 1826). In 1859 Potain became assistant professor of medicine at the University of Paris and two years later, after competitive examinations, became associate professor. Among his celebrated students were Louis-Henri Vaquez (1860–1936) and Louis-Joseph Teissier (1851–1926).

Potain was greatly interested in the graphic registration of the heart beat and pulse waves and devised an instrument which made such recordings possible. In an important study dealing with the movement of, and the sounds heard in, the jugular veins, he concluded that two varieties of murmurs are audible in the neck: namely, arterial and venous murmurs. The arterial murmurs are intermittent; the venous murmurs may be continuous, intermittent or continuous with accentuation. The accentuation or repetition of the venous murmur results only from intermittent acceleration of blood flow in the vein. The venous murmur is more likely to occur in the presence of anemia than in its absence. This work appeared in his article "On the movements and sounds that take place in the jugular veins" (translation) in 1867.

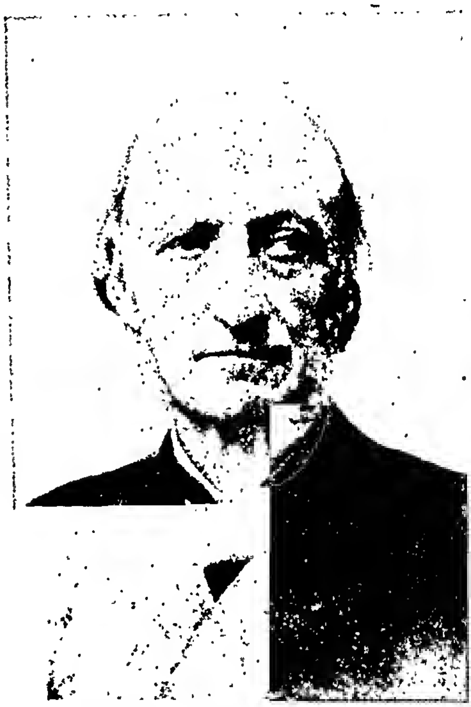
Hermann Nothnagel.

In his graphic study of gallop rhythm, a subject previously investigated by his teacher, Bouillaud, Potain concluded that this abnormal rhythm could originate in all cases in which the elastic resistance of the left ventricular wall encroaches on its muscular tonicity, either by an increase of resistance or a diminution of tonicity. This work appeared in 1885.

Potain also made precise studies on the relationship of tricuspid insufficiency and the attending circulatory disturbances, described the pulsations of the liver occurring with this valvular defect, explained the mechanism of the apex beat and recognized the localized, peculiar tympanitic accentuation of the aortic second sound which sometimes occurs in syphilitic aortitis. He named this phenomenon the "bruit de tabourka." It still today is known as "Potain's sign." He was interested

in recording arterial blood pressure and improved von Basch's manometer, which had appeared in 1881. Potain's ability to measure arterial blood pressure enabled him to demonstrate the existence of hypertension in Bright's disease, as suspected but not proved by Ludwig Traube. Potain, moreover, demonstrated that hypertension and not the impaired function of the kidneys is responsible for the frequently observed cardiac hypertrophy in Bright's disease.

His mechanical genius was demonstrated in other ways and he perfected an instrument to count erythrocytes. In studying cases in which there was pleural effusion, Potain with the aid of his assistant, Georges Dieulafoy (1839–1911), had chanced on the discovery of thoracentesis. Potain aided Dieulafoy in perfecting an aspirator with a vacuum attachment (Potain's apparatus), which is still in use. Potain soon demonstrated the practicability of this procedure in a representative series of patients. With another apparatus of his own device, Potain replaced the fluid by air progressively introduced to avoid sudden expansion of the lung. He later utilized the method of introducing air into the pleural cavity in cases of pulmonary tuberculosis and was the first, therefore, to use and advocate collapse therapy.



Pierre-Carl-Édouard Potain

In line with the greater precision in observation and the attention to more minute clinical phenomena were the observations of Heinrich Irenaeus Quincke (1842–1922), of Berlin and Kiel. The son of a prominent physician, he obtained his undergraduate medical education at the universities of Berlin, Würzburg and Heidelberg. Quincke's teachers included the anatomist, Heinrich Müller; the Swiss histologist and physiologist, Albert von Kölliker; the physiologist, Hermann L. F. von Helmholz; the chemist, Robert W. E. von Bunsen; and the celebrated pathologist, Rudolf Virchow.

Quincke received the degree of Doctor of Medicine from the University of Berlin in 1863 and two years later assisted Ernst Wilhelm von Brücke in physiology at Vienna. Quincke then visited clinics and hospitals in Switzerland, Holland, France and England. On his return to Germany he became Friedrich Theodor Frerich's (1819–1885) assistant and at the age of thirty years, in 1872, he succeeded Bernard Naunyn

(1839–1925) as professor of medicine at the University of Bern in Switzerland. In 1877 Quincke was appointed professor of medicine at the University of Kiel, where he taught until his retirement in 1908.

In addition to his contributions in pathology and physiology, he was interested in general medicine and neurology.

Quincke was the first to make detailed studies of the capillary pulse and to note its significance in the diagnosis of aortic insufficiency. He also studied the venous pulse. This work was recorded in his article, "Observations on capillary and venous pulse" (translation) and appeared in 1868. The following quotations from this article are of interest.


Heinrich Irenaeus Quincke.

There are, however, places in the human body, where under completely normal conditions, but more clearly under pathologic conditions, one frequently observes the transmission of the pulse wave from the heart reaching to the capillaries and then into the veins. These sites are the fingernails, hand, forearm and foot . . . greater amplitude and great output of individual heart contractions favor the distinctness of the capillary pulse, while marked increase in the arterial tension and greater frequency of heart contractions are less favorable. The capillary pulse will either be perceived more distinctly or (more frequently) less distinctly, according to the predominance of one or the other factor in fever and under excitement. The presence of large and rapidly falling pulsations is demonstrated in an exquisite manner in insufficiency of the aortic valves; for that reason the capillary pulse is especially distinct. . . .

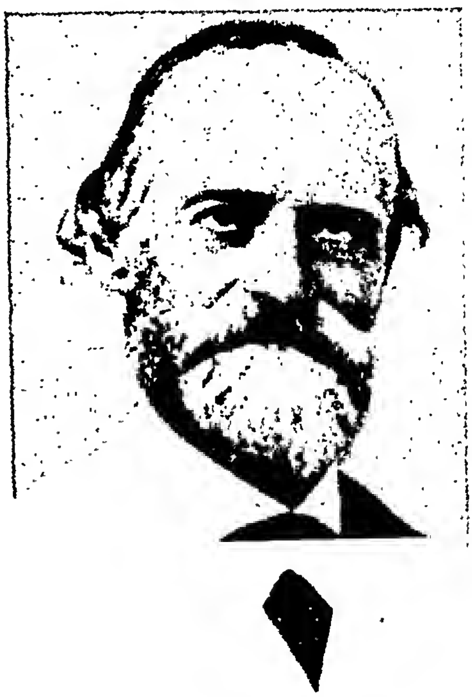
In 1870, Quincke published his observations on aneurysm of the hepatic artery and six years later contributed to the section of diseases of arteries in Hugo Wilhelm von Ziemssen's "Handbuch der speciellen Pathologie und Therapie."

In 1875 he made an important observation when he demonstrated that pressure on the carotid artery in the neck produced slowing of the heart and explained this phenomenon on the basis of stimulation of the vagus nerve. Quincke, in collaboration with Heinrich Hochhause, in 1894 discussed abortive extrasystoles (*Frustraner Kontraktion*); namely, premature contractions which are audible over the heart but are not transmitted into the peripheral arteries.

Quincke described angioneurotic edema in 1882 and for a time this condition was known as "Quincke's edema." His contributions to neurology are too numerous to mention here.

The first to associate acute endocarditis with micro-organisms gaining

entrance into the blood stream from outside the body was E. F. H. Winge (1827–1894), of Christiania (Oslo). He cited the following case reported by Malmsten in 1869 and mentioned three cases of primary endocarditis in his own experience. According to his account, a man trimmed a corn on a toe and as a result the area became inflamed and infected. There was pain, swelling and redness of the foot and a small abscess developed at the site of the injury. The patient became critically ill with chills, fever, prostration and delirium and death soon occurred with the symptoms of "blood poisoning." During the terminal phase of the illness the rapid and tumultuous action of the heart was noted and an impure heart tone or murmur was heard, which led to the opinion that the heart was diseased.



E. F. H. Winge.

At postmortem examination, the heart valves were found to be acutely inflamed and covered with cauliflower-like vegetations. The vegetations contained pus and similar small purulent lesions were found in the kidneys and spleen. In studying the pus under the microscope, Winge found minute bodies which he suggested might be parasites introduced from without the body at the time of the cutting of the corn. He reasoned that they had been conveyed by the blood stream to the valves of the heart, where they became lodged and caused the acute inflammation of these structures. Winge further reasoned that small particles of the valvular vegetations had become detached and were carried by the blood stream to the kidneys and the spleen.

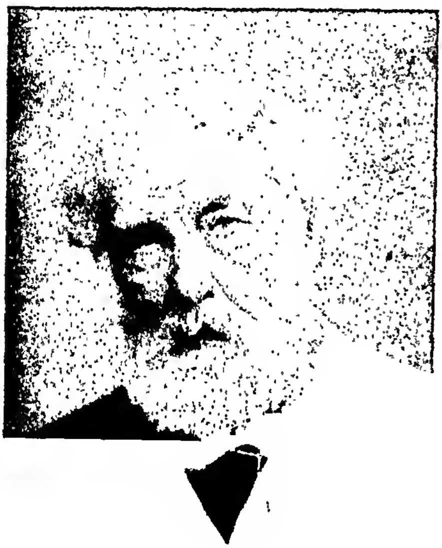
Kirkes's exposition of embolic detachments from intracardiac coagula had been reported in 1852 and undoubtedly Winge was familiar with this work. The purulent character of both the primary and secondary lesions in Winge's case in all probability indicates that he was dealing with an instance of acute bacterial endocarditis due to a staphylococcus. Winge's observations were recorded in 1870 under the title, "Endocarditis hos en man, som vårdades för pyemi."

In the same year, Sir Samuel Wilks (1824–1911), of London, gave a splendid account of bacterial endocarditis. He was apparently unaware of Winge's report, for he did not refer to the case just related. Wilks was a graduate of the University of London in 1848, became a member

of the Royal College of Physicians in 1851 and two years later was appointed physician to the Surrey Dispensary.

In 1856 Wilks was appointed assistant physician to Guy's Hospital, the clinic where Richard Bright (1789–1858) was consulting physician and Thomas Addison (1793–1860) was an attending physician. At Guy's Hospital, Wilks served as pathologist and curator of the museum and became full physician in 1867.

Among his many important contributions was the account of bacterial endocarditis, "Capillary embolism or arterial pyaemia," 1870. The following quotation from this article is of interest.



Sir Samuel Wilks.

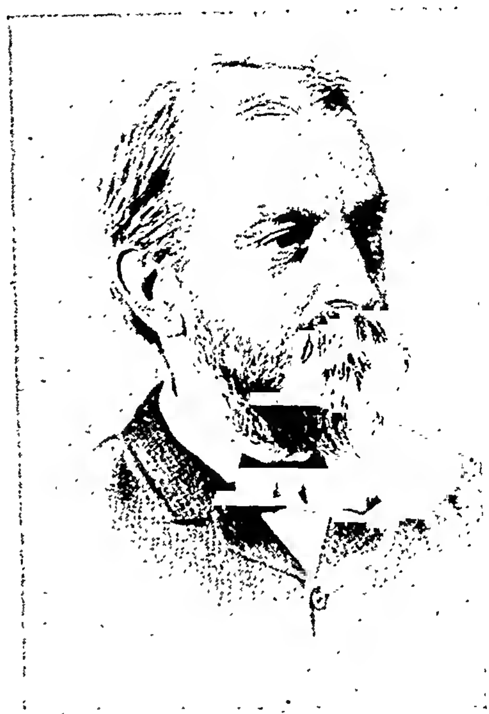
> I would say, therefore, that arterial pyaemia is a by no means uncommon affection and that it is seen frequently in chronic heart disease; but the symptoms are overshadowed by the more severe ones attendant on the valvular imperfections, or if observed, regarded merely as rheumatic. Also, that it may be often met with where there is no history of a primary heart affection, although an endocarditis at the time of the occurrence of the symptoms may exist. Also that it should be suspected in cases of obscure febrile conditions, especially if accompanied by rigors, and more especially where the liver and spleen have been found to be slowly increasing in size.

Wilks published his "Lectures on pathological anatomy" in 1859 and in 1863 published a paper "On the syphilitic affections of internal organs." He was one of the first to investigate and describe visceral syphilis and described aortic aneurysms among soldiers infected with syphilis. Wilks ascribed the myocardial changes in syphilis to two causes, gummata and obliterative endarteritis. He became interested in diseases of the nervous system and published his comprehensive work on this subject under the title of "Lectures on diseases of the nervous system," in 1878.

Important physiologic investigations were conducted by Adolf Fick (1829–1901), of Kassel. He was a physiologist of note and a pupil of the celebrated Carl Ludwig. Fick was particularly interested in the physiology of muscles and in hemodynamics. He was possessed of unusual ingenuity in the creation of apparatus to carry out his experimental studies. Among these innovations was a cosine lever, a myotonograph and an improved thermopile. In 1870, Fick conducted extensive studies on blood flow and later (1882) investigated methods of estimating the work and the output of the heart. He also measured the pressure within

the chambers of the heart. While Fick's conclusions were not correct in all respects he nevertheless contributed to a clearer understanding of many of the complex problems of hemodynamics.

One of the pioneer physiologists of America was Henry Pickering Bowditch (1840–1911), of Boston. He was the founder of the first physiologic laboratory in the United States in 1871. Bowditch's contributions to the physiology of muscles and especially to that of the heart muscle were of fundamental importance. In his experimental work on the myocardium by direct electrical stimulation of uniform intensity and frequency he found that the first few contractions decreased slightly but after this initial fall, the contractions increased with remarkable regularity. This gradual increase in the extent of muscular shortening with a constant stimulus led him to name this behavior "treppe" or staircase phenomenon. After this period had been passed, the contractions were found to diminish steadily until muscular fatigue ensued and no further response to stimulation occurred.



Henry Pickering Bowditch.

Bowditch also demonstrated the important fact that the heart liberates all of its available energy at each contraction, as in the explosion of gunpowder. Thus, the strength of the cardiac contraction depends on the amount of energy stored in the muscle and the contraction is always maximal. This phenomenon is known as the "all or none" law of Bowditch.

By ingenious experiments on the exposed sciatic nerves of anesthetized cats, Bowditch proved the indefatigability of nerves. Shielded electrodes were placed on the nerve, a lever recording apparatus was devised for registering muscular contractions and curare was administered to the animal. During the action of the drug no muscular response occurred to continuous induction stimulation but after one and a half to two hours, muscular twitchings appeared. Another effective dose of curare was administered and after a total period of stimulation covering four hours, muscular twitching again occurred when the effect of the curare had worn off. This led Bowditch to conclude that the nerve was indefatigable. These experiments were the first demonstration of functional nerve block by means of a drug and opened the portals for the future development of nerve block anesthesia.

One of the outstanding clinicians and teachers of this period was Jacob Mendes DaCosta (1833–1900), of Philadelphia. A student of the celebrated Frenchman, Armand Trousseau (1801–1867), DaCosta did much to instill vigor and imagination into American medical teaching.

He gave the first accurate account of neurocirculatory asthenia, based on data which he had acquired from observations on soldiers during the Civil War. This article, "On irritable heart; a clinical study of a form of functional cardiac disorder and its consequences," appeared in 1871. DaCosta reported on approximately 300 cases and commented that he had observed identical cases in private practice. He stated that soldiers who had recovered from digestive disturbances and diarrhea, which were frequent among the troops, and had returned to active duty were unable to withstand the exertions demanded of them. The following quotation illustrates this point.

Jacob Mendes DaCosta.

> He soon noticed that he could not bear them as formerly; he got out of breath, could not keep up with his comrades, was annoyed with dizziness and palpitation and with pain in his chest; his accoutrements oppressed him and all this though he appeared well and healthy. Seeking advice from the surgeon of the regiment, it was decided that he was unfit for duty, and he was sent to a hospital, where his persistently quick acting heart confirmed his story, though he looked like a man in sound condition. . . .

DaCosta was of the opinion that severe or recurrent muscular activity was capable of producing cardiac hypertrophy (so-called athlete's heart).

Clinical teaching in Philadelphia until DaCosta's time (1866) was very inadequate. The mode consisted of literally memorizing a textbook and being able to pass examinations. Actual bedside instruction was not emphasized until DaCosta set the pattern in his brilliant method of teaching.

A gifted teacher, a sound clinician and an able investigator, these terms describe Ludwig Traube (1818–1876), of Berlin. He was a pioneer in experimental pathology and made numerous important contributions to the field of cardiology. Among Traube's teachers were Johannes Evangelista Purkinje (1787–1869), Johannes Müller (1801–1858), Josef Skoda (1805–1881), Carl Rokitansky (1804–1878) and Johann Lucas Schönlein (1793–1864).

Traube received the degree of Doctor of Medicine from the University of Berlin in 1841 and then engaged in graduate study in Vienna. He established practice in the suburbs of Berlin but, like other young physicians, was denied teaching and postmortem resources. At times he was obliged to pay a fee for the privilege of performing a necropsy. In spite of these handicaps, Traube's reputation grew and he was soon in demand as a private lecturer. In 1849, through the influence of Virchow, Traube received his first hospital appointment as assistant to Schönlein and in 1857 became an associate at the Charité and assistant professor at the University of Berlin. Even though his great ability was widely recognized, Traube did not receive his full professorship until 1872.

One of Traube's classic contributions dealt with a concise description of pulsus bigeminus, its mechanism and significance. The following quotations are in translation.

The nature of the pulsus bigeminus may be said to be this: following every two pulses which originate in the aorta, a longer pause ensues. This phenomenon is differentiated from the pulsus dicroticus by the fact that in the latter there is only one contraction of the heart for every two beats of the pulse, while in pulsus bigeminus there are two contractions of the heart, which follow one another rapidly and are separated from the preceding and succeeding contractions by a longer pause. For every two beats of the pulsus dicroticus there occur, as in the normal pulse, only two heart tones, while in pulsus bigeminus four tones are audible. . . .

Ludwig Traube.

Traube produced pulsus bigeminus experimentally by curarization of the animal and section of the vagi.

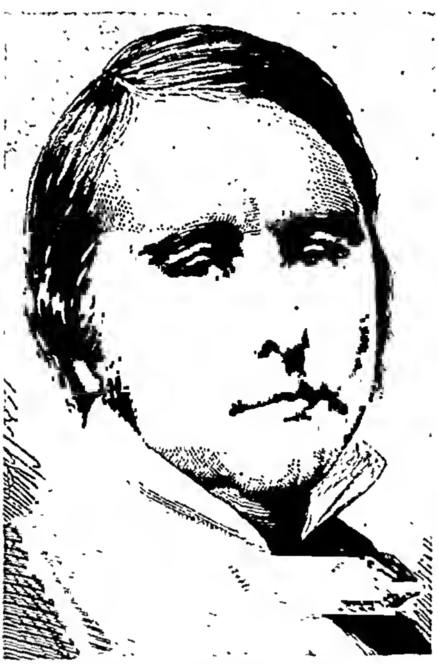
. . . I concluded from these facts, that two conditions are necessary for the appearance of the pulsus bigeminus.

(1) The heart must be released from the influence of the inhibitory spinal nervous system and also

(2) There must be some agent circulating in the blood, which increases the irritability of the cardiac component of the inhibitory spinal nervous system, which is still functional.

He concluded that the phenomenon occurs with failure of the left ventricle and cited an instance in which digitalis apparently contributed to its appearance. This work appeared in 1871 under the title, "Ein Fall von Pulsus bigeminus nebst Bemerkungen über die Leberschwellungen bei Klappenfehlern und über acute Leberatrophie."

Earlier, in 1856, Traube had published a comprehensive account of the relationship of cardiac and renal disease which appeared as "Über den Zusammenhang von Herz und Nieren Krankheiten." He described renal congestion of cardiac origin and distinguished these changes from inflammatory diseases. Traube also described the symptomatology of contracted kidney and explained the associated hypertrophy of the heart as being the result of increased circulation observed by the diminution of the number of renal capillaries. He discussed Cheyne-Stokes respiration and attributed this phenomenon to a diminished supply of arterial blood to the medulla which resulted in the deprivation of the respiratory center of an adequate amount of oxygen. In 1847, Traube investigated the parenchymal changes in the lungs following section of the vagi.



Sir William Withey Gull.

When Traube was fifty-six years of age coronary disease developed with the anginal syndrome, which finally eventuated in congestive heart failure. He diagnosed his own disease as "hypertrophy and dilatation of both ventricles with arteriosclerosis and coronary sclerosis with partial fatty degeneration of the myocardia." His death occurred from congestive heart failure in 1876 at the age of fifty-eight years.

Three years after the publication of Winge's classic account of acute bacterial endocarditis, Hjalmar Heiberg (1837–1897), professor of pathologic anatomy at the University of Christiania (Oslo), recorded a similar case. The patient was a young woman twenty-two years of age who showed symptoms and signs of sepsis ten days after childbirth. Chills and fever occurred with painful swelling of the elbows, shoulders and right knee, and an erysipeloid eruption in the right axilla developed. Multiple small abscesses appeared in the skin of the extremities. The patient became stuporous and died thirty-five days later.

At postmortem examination, Heiberg found ulcerative endocarditis involving the mitral valve with infarcts in the spleen and kidneys. The kidneys were also the seat of miliary abscesses. A large gangrenous swelling containing pus was found under the mandible. Heiberg suggested that the infectious process might be due to Leptothrix. Tissue was sent to Virchow, who commented on Heiberg's report but con-

tended that Leptothrix was not the infecting agent. Virchow asserted that it was a minute body and according to the older terminology would have been classified as a species of Vibrio. He could not identify the little bodies but stated that he could not disprove their parasitic nature.

Heiberg's work appeared under the title, "Ein Fall von Endocarditis ulcerosa puerperalis mit Pilzenbildungen im Herzen (Mycosis endocardii)," 1872.

One of the most brilliant clinicians and pathologists of this period of the century was Sir William Withey Gull (1816–1890), of Colchester and London. A graduate of the University of London in 1846, he became associated with Guy's Hospital soon after completing his medical course. Here he continued to teach medicine and conduct research throughout the rest of his life.

Gull's outstanding contribution with reference to the cardiovascular system was produced in collaboration with Henry G. Sutton. In this work, based on careful clinical observations with postmortem and microscopic correlations, they were the first to promote and prove the concept of primary arteriolar disease in what was then referred to as chronic Bright's disease. While no mention was made of blood pressure, their clinical observations having been conducted before practical methods of measurement were available, they nevertheless were very close to discovering the existence of hypertension in the cases they had studied.

Gull and Sutton were primarily interested in the cases displaying what they referred to as "hyalin-fibroid" in the arterioles and capillaries. They particularly stressed the point that these changes were not confined to the vessels of the kidney but also occurred primarily in other organs such as the heart, lungs, aorta, brain, retina, spleen, stomach and even in the vessels of the skin.

They insisted that the contraction and atrophy of the kidney were not the cause of the generalized vascular changes but were only a manifestation of the generalized process. Furthermore, Gull and Sutton were emphatic in their statements that the diffuse vascular lesions did not result from impaired function of the kidneys. They called attention to the almost universal hypertrophy of the left ventricle in cases showing diffuse arteriolar changes while in many cases of primary renal disease, hypertrophy of the left venticle did not occur. It was here that the concept of existent hypertension might have been realized.

Not certain of the true nature of the pathogenesis of the vascular lesions, Gull and Sutton noted that while the lesions appeared to be related to senile changes, their distinct causes were as yet undetermined. Gull and Sutton referred to the vascular lesions as "arterio-capillary fibrosis."

The following quotation from this work is significant.

> Clinical medicine, especially as followed in private practice, enables us often to predict and trace these changes onwards until the morbid formation is general. Thus, a patient may come under care for headache and other allied symptoms in whom, at a given stage, the renal and cardiac functions may be normal, and as the case goes on the urine first or the heart first, or the breathing may first give signs of further lesion until, as the malady progresses, that state called chronic Bright's disease with contracted kidney may be fully produced, as shown by the thickened heart, the pale watery urine, the shrunken skin, the troubled brain and the dimmed sight.

This monumental work appeared in 1872, titled, "On the pathology of the morbid state commonly called chronic Bright's disease with contracted kidney ('arteriocapillary fibrosis')."

Gull also contributed other important studies and was one of the first to observe the posterior spinal lesions in tabes dorsalis (1856–1858). He described intermittent hemoglobinuria in 1866, recorded accounts of vascular obstructions, cerebral abscess, anorexia nervosa and factitial urticaria and with Thomas Addison (1793–1860) described the lesions of xanthelasma. Gull was a pioneer in the use of male fern in tenia infestation (1855) and of static electricity in the treatment of nervous diseases (1852).

An interesting account of the compression treatment of abdominal aneurysm was reported by Walter Moxon (1836–1886) and Arthur Edward Durham (1834–1895), of London. Moxon was assistant physician and lecturer on morbid anatomy at Guy's Hospital and Durham was surgeon and lecturer on anatomy at the same hospital.

They reported the case of a young man having an aneurysm of the abdominal aorta in which the following treatment was applied. The patient received rest in bed for eleven days, during which time a light diet was prescribed and pills of lead acetate and opium were administered every six hours to aid in curbing the appetite. Then, with the patient under chloroform anesthesia, an abdominal tourniquet was applied and gradually screwed in position until the pulsations of the aneurysm were completely arrested but special attention was given not to exert more pressure than was necessary.

During this procedure, the pulsations in both femoral arteries became absent. The limbs were enveloped in cotton wool and flannel and hot water bottles were applied. The patient was kept under chloroform anesthesia and the pressure was maintained for ten and a half hours. The treatment was then terminated. When the tourniquet was removed, the aneurysm no longer pulsated and was apparently smaller and harder than before. However, later, pulsations in the epigastric region returned but gradually became less marked. After three months of complete rest in bed, the patient was gradually permitted to be up and about. The authors concluded that they had effected a cure by producing thrombosis within the sac of the aneurysm.

Moxon and Durham published their article, "Case of abdominal aneurism cured by compression of the aorta," in 1872.

An able German clinician, Adolf Kussmaul (1822–1902), made numerous important contributions to medicine, including interesting observations on pericarditis. A graduate of the University of Heidelberg, he served as an army surgeon for two years and then engaged in private practice for several years. Attracted by the brilliant teacher, Rudolf Virchow, who was at that time in Würzburg, Kussmaul matriculated there and in due course of time received his doctor's degree. His fame spread rapidly and in 1857 he became professor of medicine at Heidelberg. Two years later Kussmaul accepted the chair of medicine at Erlangen, at Freiburg in 1863 and at Strasbourg in 1876.

Adolf Kussmaul.

Kussmaul noted a peculiar pulse in adherent pericarditis which he named the "pulsus paradoxus." This consisted in a marked diminution of the pulse wave during inspiration, occasionally resulting in the actual dropping of a beat during this period. This phenomenon was not claimed to be a constant accompaniment of adherent pericarditis and strands of adhesions about the aorta and the venae cavae were believed to be responsible. Griesinger was the first to mention this peculiar pulse (1854) but did not record his findings. It was reported, however, by A. Widenmann in 1856 with credit to Griesinger. Kussmaul's article appeared in 1873 under the title "Ueber schwielige Mediastino-Pericarditis und den paradoxen Puls."

Kussmaul's contributions were varied. He conducted a study on the changes of color in the eye in 1845, on the influence of the circulation on the movements of the iris in 1856 and on the relation between anemia and epileptiform convulsions in 1857. Two years later he produced a monograph on the psychology of the newborn infant, in 1861 wrote on salivation during the administration of mercury and in 1877, on disorders of speech. Kussmaul was the first to describe periarteritis nodosa in collaboration with Rudolf Maier in 1866 and progressive bulbar palsy in 1873. He described diabetic coma associated with acetonemia and the peculiar concomitant air hunger (still known as "Kussmaul's air hunger") in 1874. He made the first clinical diagnosis of mesenteric

embolism (1864), was the first to attempt esophagoscopy and gastroscopy (1869), the first to perform lavage of the stomach with a tube for dilatation and the first to employ bismuth in the treatment of gastric ulcer. Kussmaul was also a pioneer in performing thoracentesis (1868).

Kussmaul's autobiography, "Jugenderinnerungen eines alten Arztes," (The youthful recollections of an old physician), is one of the most clever accounts of this nature ever written.

Probably the first authenticated account of the successful removal of a foreign body from the human heart is that of George William Callender (1830–1878), surgeon to St. Bartholomew's Hospital in London. In 1873 he reported the case of a thirty-one year old pewterer into whose chest a long needle, which had been stuck in the left side of his coat, was plunged during a fight. The man experienced momentary pain, missed the needle and the following morning sought medical advice. No puncture wound was found and the patient was dismissed. Nine days later he sought re-examination because of pain in the left thoracic wall extending from the left nipple to the axilla. The pain was continuous and the patient also complained of palpitation.

George William Callender.

Callender noted a slight fullness in the left intercostal space near the location of the apex beat and, with the patient under chloroform anesthesia, explored this area. The needle was encountered moving in an arc with each beat of the heart. It was withdrawn in its entirety except for the eye. The length of the needle was 1 9/10 inches (4.8 cm.). The patient made an uneventful recovery. This interesting report was published in 1873 in Callender's article "Removal of a needle from the heart. Recovery of the patient."

Callender commented on a previous publication (without bibliographic reference) of Georg Fischer, who had collected a group of thirteen cases in the literature of foreign bodies in the heart, chiefly needles and pins. Most of them were discovered at postmortem examination and Callender contended that in the two cases in which operation was performed, no definite proof was presented regarding the actual entrance of the foreign body into the heart.

The near recognition of cardiac infarcts is revealed in an interesting

study conducted by Charles Hilton Fagge (1838–1883), of Hythe and London. A physician to Guy's Hospital, he was an able clinician and pathologist and at one time was editor of the Guy's Hospital Reports.

In 1874, Fagge published his report on eleven cases of heart disease in which postmortem examination and microscopic study of the heart revealed "fibroid" changes. He was referring to myofibrosis. He described the frequent patchy character of the lesions and the extreme thinness of the wall of the ventricle in certain cases. The following statement is so significant that it is quoted directly from Fagge's article. ". . . For it is to be observed that this affection never attacks the whole heart at once, nor even the whole of a single chamber. It is always more or less localised, and sometimes invades only a very small tract. . . ."

He clearly described ventricular aneurysms: ". . . When the whole thickness of the heart's wall at any point has become completely replaced by fibrous tissue this is generally much thinner than the rest of the chamber. It then probably always shows more or less decidedly a tendency to bulge and to form a pouch, and in some cases this leads to the formation of distinct aneurysms of considerable size. . . ."

No mention of the coronary arteries or their condition was recorded in any instance but Fagge emphasized the points that nine of the eleven patients were male and that most of them were forty years of age or older. Death occurred suddenly in three cases. Most of the patients were admitted to the hospital in congestive heart failure. No comments were made regarding previous painful thoracic seizures. No definite etiologic factor was offered for the fibrous changes although Fagge discussed the possibility of inflammatory effects from pericarditis and endocarditis, syphilis and arteritis. Had the coronary arteries been carefully studied, he undoubtedly would have conceived the relationship between obliterative coronary disease and healed and healing myocardial infarcts.

This interesting article appeared under the title, "A series of cases of fibroid disease of the heart," in 1874.

Fagge also investigated cretinism and rachitis and was a dermatologist of note. In the latter field he classified keloid, morphea and spurious leprosy under the term, "scleriasis," in 1867. He gave a classic account of gastromesenteric ileus in 1869. His large work, "Principles and practice of medicine" (1885–1886), was completed by Henry Pye-Smith (1840–1914) and Sir Samuel Wilks (1824–1911) after his death.

An important article based on careful clinical observations was contributed by an English Army Surgeon, Francis H. Welch (1840–1910). In addition to his military duties, he was assistant professor of pathology of the Army Medical School at Netley. Welch's work was communicated by Dr. George D. Pollock, on November 23, 1875, to the Royal Medical and Chirurgical Society of London. This communication received little attention at the time but was credited by Osler as being

the most authoritative treatise on aortic aneurysm ever written in the English language up to its time. The title of the article was "On aortic aneurism in the army, and the conditions associated with it."

Welch reported on his findings among the soldiers of the British Army. He described a "fibroid" lesion, affecting chiefly the internal coat of the aorta, which, he stated, as a rule ultimately disintegrates. He believed that it was largely concerned with syphilis but that rheumatism and alcoholism might also play a lesser role in its origin. The lesion may not be progressive but if extensive and severe, it becomes progressive and eventuates in one of three fatal phases: formation of aneurysm, involvement of the aortic valve or hypertrophy, with or without dilatation of one or more of the chambers of the heart.


Carl Rokitansky.

Welch also described another change in the intima of the aorta "characterized by limited opacity or fatty change of the normal textures." This, he believed, occurred chiefly with destructive changes in the lungs but rarely led to serious consequences. He criticized the military uniforms and believed that tight garments produced constriction of the chest and that this together with physical exertion was a secondary cause of aneurysm.

Another important contributor to cardiology was the brilliant Bohemian pathologist, Carl Rokitansky (1804–1878), for many years professor of pathology at Vienna. A close friend of Joseph Skoda (1805–1881), he was said to be largely responsible for Skoda's success. Rokitansky had four sons, two of whom became physicians and two singers. He remarked jestingly on occasions that "Die Einen heilen, die Anderen heulen" (the first heal, the others howl). An inspiring teacher and a keen observer, he is said to have performed at least 30,000 postmortem examinations during his active years.

Rokitansky's most noted work on the heart comprised his observations and descriptions of congenital defects of the cardiac septum. After fourteen years of careful investigation he expounded his transposition hypothesis of the deviation of the aortic septum. He showed that the ventricles in their development are separated from each other by the upward growth of the septum and that the common arterial trunk is also separated into right and left halves by a septum having its origin

in an indentation in the walls of the vessel. The septum of the ventricles and the septum between the two halves of the arterial trunk become joined, so that each ventricle finally communicates with one half of the vessel. Normally, a rotation of the arterial ends of the ventricles and the great arterial trunk occurs so that the portion of the trunk destined to become the pulmonary artery is in front and to the left of that portion destined to become the aorta. If in the course of development this process of rotation fails to occur prior to the union of the ventricular and aortic septa, it becomes possible for the aortic portion of the trunk to open into the right ventricle, while the pulmonary portion communicates with the left ventricle.

This monumental work appeared in Rokitansky's volume "Die Defekte der Scheidewände des Herzens," Vienna, 1875.

In an earlier work, "Ueber einige der wichtigsten Krankheiten der Arterien," 1852, he had described atheroma and calcification in the intima of arteries.

Rokitansky was the first actually to demonstrate the presence of micro-organisms in the vegetations of acute endocarditis although Winge in 1870 had observed microscopic bodies in vegetations which he suggested might be parasites. Rokitansky was also one of the first to make microscopic studies of the fatty heart.


Sir William Richard Gowers.

Among Rokitansky's other contributions was his distinction between lobar pneumonia and bronchopneumonia (lobular pneumonia), the distinction between Bright's disease and amyloid degeneration of the kidney (Speckniere), his account of acute dilatation of the stomach (1842), his description of acute yellow atrophy of the liver (1843) and many others.

Pre-eminently a neurologist, Sir William Richard Gowers (1845–1915), of London, made an important study which was related to the heart and blood vessels. He graduated from University College, London, and in 1867 qualified for membership in the Royal College of Surgeons. In 1869 Gowers received the degree of Bachelor of Medicine from the University of London, and a year later the degree of Doctor of Medicine, and was awarded the gold medal for exceptional scholarship. Following his graduation, he was appointed registrar to the

National Hospital for the Paralysed and Epileptic and was also private secretary to Sir William Jenner. Following other appointments, Gowers was ultimately appointed professor of clinical medicine at the University Medical School.

Gowers was one of the pioneers in the use of the ophthalmoscope and in this field contributed an important study pertaining to the vascular system. This work was published in his article, "The state of the arteries in Bright's disease," in 1876. In studying the ocular fundi of patients who had Bright's disease he confirmed his impressions of the coexistence of hypertension (by means of palpation of the radial pulse) with vascular changes in the retina. Gowers found a close correlation between constriction of the retinal arterioles and increased arterial pressure. He stated:

> The practical use of inspection of the retinal vessels is perhaps less than its pathological value, but it is, I think, considerable. It is true we can generally ascertain the amount of arterial tension more readily and more surely by feeling the pulse than by looking at the retinal vessels. But sometimes the incompressibility of the pulse cannot readily be estimated, on account of its smallness and the amount of subcutaneous fat or oedema. In these cases, retinal inspection may be useful. Moreover, as affording definite information regarding the pathological processes in different cases of Bright's disease, it will, I think, have considerable value, and some facts which have come under my observation, at present too few and isolated for more than mention, make one hope that ultimately it may help us better to distinguish between morbid states included under the term and at present imperfectly distinguished.

Gowers' last sentence proved to be a remarkably accurate prophecy.

In neuro-anatomy, Gowers discovered the tract of fibers in the gray matter in the anterior and lateral funiculus of the spinal cord, known as "Gowers' tract." This work appeared in a lecture of 1879, "The diagnosis of diseases of the spinal cord." He also established a method of determining the percentage of hemoglobin and the number of corpuscles in the blood.

In 1885 he published his book, "Lectures on the diagnosis of diseases of the brain," in which he correlated his own findings with those of Hughlings Jackson (1834–1911), Paul Emil Flechsig (1847–1929), Eduard Hitzig (1838–1907) and David Ferrier (1843–1928). These are but a few of Gowers' important contributions.

A pioneer in the study of blood pressure and the creator of a sphygmograph was the celebrated French physiologist, Étienne-Jules Marey (1830–1904), of Paris. His work, however, was preceded by Karl Vierordt's imperfect attempts by twenty-one years (1855).

Marey devised the first reasonably useful apparatus for estimating the arterial blood pressure in man. The hand of the subject was placed in a plethysmograph connected with a bottle devised for raising the pressure and a sphygmoscope tambour for recording the size of the pulse waves. This work appeared in 1876 in an article titled, "Pression

et vitesse du sang." Two years later another report appeared, "Nouvelles recherches sur la mésure manometrique de la pression du sang chez l'homme." In this work Marey stated that the maximal pressure (systolic) may be determined as the point where the pulsation disappears and the minimal pressure (diastolic) as the point where the oscillations are of greatest magnitude.

Marey's instrument regrettably was neither precise nor practical but it did permit a registration of the rhythm of the heart and form of the pulse waves. Marey demonstrated the fundamental fact that the maximal excursion of the pulse wave was obtained when the pressure about the artery was equal to the pressure within the artery. In devising his sphygmograph he attempted to avoid the errors of inertia by using a very light recording stylus.

Étienne-Jules Marey.

In 1860 Marey had devised the first polygraph, which consisted of an ordinary kymograph drum arranged to rotate horizontally with two tambours arranged to inscribe a record on the drum. Two simultaneous records could be obtained from the jugular vein and the carotid artery or from one of these vessels and the apex beat of the heart. This instrument, however, lacked mechanical precision but undoubtedly formed the basic concept for his later apparatus.

A renowned pathologist and clinician of the German school of medicine was Julius Friedrich Cohnheim (1839–1884), of Kiel and Berlin. A graduate of the University of Berlin, he also studied at Würzburg before his graduation. He received his training in histology under Albert von Kölliker and in pathology under Rudolf Virchow and became intimately associated with Friedrich von Recklinghausen and Edwin Klebs. His graduation thesis, "De pyogenesi in tunica serosis," was prepared under the direction of Virchow. In 1862 he worked with Ludwig Traube and gained experience in experimental physiology under this great teacher. Cohnheim accepted an assistantship to Virchow and remained with him for seven years, although this tenure was temporarily interrupted by the German-Danish War, in which he served in the army. In 1868, when only twenty-nine years of age, he became professor of pathology at the University of Kiel. Four years later he accepted a

call from the University of Breslau. In 1878 he became professor of general pathology and pathologic anatomy at the University of Leipzig.

Cohnheim is particularly known for his experimental work on the coronary arteries conducted in collaboration with his student, von Schulthess-Rechberg. In these experiments the coronary arteries of curarized dogs were obstructed by the application of clamps and the effect of this procedure was investigated. The authors concluded that the mechanical obstruction of either main coronary artery caused the ventricles to become arrested in diastole within a period of two minutes. This led them to accept the belief that the coronaries were end arteries and that if any anastomoses existed they must exist in the form of minute capillaries. These conclusions were accepted as realities for many years. This work appeared as "Ueber die Folgen der Kranzarterienverschliessung für das Herz," 1881.

Julius Friedrich Cohnheim.

In 1877, Cohnheim made his important contribution on paradoxical embolism, which appeared in his lectures on "General pathology" (translation). The following quotation is in translation from this work:

> Thus I had quite lately an opportunity of observing a case of recent fatal embolism of one of the mid. cerebrals in a woman thirty-five years of age where the valves of the heart, aorta ascendens, in short all the arteries from which an embolus might have been conveyed, were absolutely intact, while on the other hand an extensive thrombosis had occurred in the veins of the lower extremity. I had not, as you may suppose, at first the remotest idea of connecting the two conditions, till on more carefully inspecting the heart, I discovered a *foramen ovale* so large that I could easily pass three fingers through it. I could not any longer reject the possibility that here a thrombus carried off from the *v. femoralis* had on its way through the heart passed from the right into the left auricle and thence into the mid. cerebral.

Many other contributions to the field of pathology were products of Cohnheim's fertile mind and intensive efforts. He was one of the first exponents of the belief that the normal heart is possessed of great amounts of reserve power, he described sudden death from coronary embolism, commented on the so-called idiopathic hypertrophy of the heart and contended that cyanosis and edema occurring in cases of pericardial effusion were due to stasis of blood interfering with the proper oxygenation of the blood.

Cohnheim showed that when large quantities of sodium chloride were introduced into the blood stream of dogs, increased transudation of fluid into the tissues occurred. Whether the significance of this basic observation was appreciated in terms of present-day concepts of fluid retention in heart failure, is impossible to state.

Additional clinical data with reference to angina pectoris were contributed by Sir William Tennant Gairdner (1824–1907), of London, a prominent physician. He was the first to call attention to the painless form of angina pectoris which he designated as "angina pectoris sine dolore." Gairdner described the sudden onset of a sense of impending death unaccompanied by any painful sensation in patients who previously had suffered from typical attacks of angina pectoris. He called attention to the fact that these painless episodes at times terminated in death. These observations were published under the title, "Angina pectoris and allied states; including certain kinds of sudden death," in J. R. Reynolds' "A system of medicine," 1877.

Sir William Tennant Gairdner

An ingenious device used for many years in the treatment of heart failure was invented by Reginald Southey (1835–1899), of London. His medical education was acquired at St. Bartholomew's Hospital and in 1860 he became a member of the Royal College of Physicians. In the same year, Southey was elected Radcliffe Travelling Fellow and in 1861 received his Bachelor of Medicine degree from the University of Oxford. He spent a year on the Continent studying in hospitals and clinics in Berlin, Prague and Vienna and subsequently visited South America.

In 1865 Southey was appointed assistant physician to St. Bartholomew's Hospital and five years later was promoted to full physician and lecturer on public health and medical jurisprudence in the Medical School. In 1866 he received the degree of Doctor of Medicine from Oxford. In 1877 he introduced trocar-like tubes to be inserted into the tissues of edematous limbs in cases of anasarca to permit the escape of fluid. These cannulae became known as Southey tubes and are still mentioned in modern textbooks. Their use, however, has been virtually abandoned since the introduction of the mercurial diuretics although they served a useful purpose in cases of refractory edema in years past.

The first correct diagnosis of coronary thrombosis made during the life of the patient was made by Adam Hammer (1818–1878), of St. Louis, Missouri, and Vienna. Born in Mingalsheim, Baden, he received the degree of Doctor of Medicine from the University of Heidelberg in 1842. A participant in the Revolution of 1848, which failed, Hammer was obliged to leave Germany and sought refuge in America, arriving in St. Louis in the autumn of the same year. According to Major, he established practice and was granted a charter by the Missouri Legislature in 1850 to establish a medical school. This school was in existence only one year but nine years later Hammer organized another, the "Humboldt Institut," where instruction was conducted solely in the German language. Its existence lasted ten years. In 1877 Hammer returned to Europe and in 1878, the year of his death, practiced medicine in Vienna.

Adam Hammer.

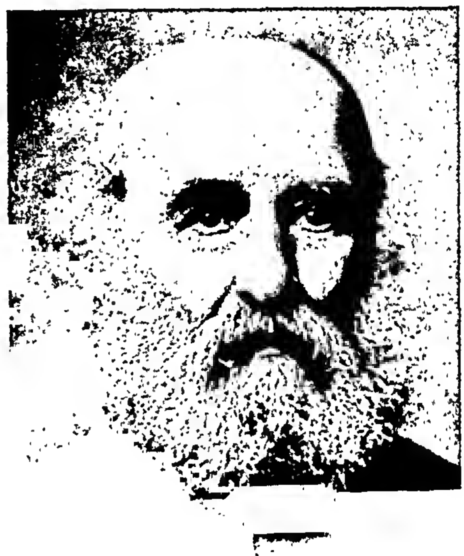
Hammer's case report of coronary occlusion, verified by postmortem examination, appeared in 1878 under the title, "Ein Fall von thrombotischem Verschlusse einer der Kranzarterien des Herzens. Am Krankenbette konstatirt." Unfortunately this important observation attracted little attention although Herrick referred to the article in his report of 1912.

A contribution dealing with the astute utilization of percussion was recorded by Thomas Morgan Rotch (1849–1914), of Philadelphia and Boston. He received his medical degree from Harvard Medical School in 1874 and then spent two years on the Continent studying at Berlin, Vienna and Heidelberg. Rotch returned to Boston in 1876, established practice and became the first pediatrician in this area. In 1888, he became professor of diseases of children in the newly opened department at Harvard Medical School and was an American pioneer in infant feeding.

Rotch described a sign which he believed to be the first objective evidence of pericardial effusion and to be manifested before the effusion became massive. In fact he believed that quantities of fluid as little as 70 to 80 c.c. could be detected by his method. He conducted experiments on cadavers where he introduced melted cocoa butter into the intact pericardium, allowed it to solidify and then after insufflation of

the lungs demonstrated absence of resonance on percussion in the fifth right intercostal space. Rotch reported on three cases in which his method permitted him to detect the presence of pericardial effusion before more striking evidences appeared. This article was published in 1878 under the title: "Absence of resonance in the fifth right intercostal space diagnostic of pericardial effusion." Even today, this area of percussion dullness is referred to as "Rotch's sign."

Sixteen years after Raynaud's description of the vasomotor disorder later to be known by his name, a famous American physician, Silas Weir Mitchell (1830–1914), of Philadelphia, also described a vasomotor disease of the extremities. The son of a prominent physician, Dr. John K. Mitchell, professor of medicine at Jefferson Medical College, young Mitchell graduated from this college in 1850. He then spent a year securing graduate study in France and on his return to America assisted his father in practice, served in military hospitals in Philadelphia during the Civil War and then established his own practice in his native city.



Thomas Morgan Rotch.

Early in his life, Mitchell wrote both prose and poetry and most of his writings appeared under pseudonyms. In 1898 his famous novel "Hugh Wynne" was published and became widely acclaimed as a literary masterpiece.

In 1872 and again in 1878, Mitchell described the vasomotor disturbance which became known as erythromelalgia. The earlier publication attracted little or no notice. The later article appeared under the title, "On a rare vaso-motor neurosis of the extremities, and on the maladies with which it may be confounded." Brief quotations from this article are of interest particularly because present-day clinicians are not in accord as to the existence of the disorder as a specific entity.

> . . . The patient, nearly always a man, after some constitutional disease, like a low fever, or after prolonged physical exertion afoot, begins to suffer with pain in the foot or feet; usually it comes in the ball of the foot, or of the great toe, or in the heel; and from these parts it extends so as to involve a large portion or all of the sole, and to reach the dorsum, and even the leg. More often it is felt finally in a limited region of one or both soles, and does not extend beyond these areas. At first it is felt only towards night, and is eased by the night's rest; but, soon or late, it comes nearer and nearer to the hour of rising from bed. In like manner, while at first it is made to increase only by excessive exertion afoot, by and by it comes

on, whenever the upright posture is assumed, or even when the foot is allowed to hang down. Since, however, the disease is not necessarily progressive, there are instances in which the pain never passes a definite limit. . . .

In later stages of the disease the pain is throbbing, aching, and burning, owing, I suppose, to the vasal disorders, which are seen in some cases throughout, and always in the graver examples.

In every case and at all stages, the pain is relieved or arrested by the horizontal position, and by cold. It is brought on and made worse by standing or walking; and, in bad cases, by allowing the feet to hang down; while warmth, and, of course, heavy feet-covers, act in a like manner. Summer is usually, not always, the season of greatest annoyance; winter a time of comparative ease. The sufferer sleeps with uncovered feet, and goes about without stockings in his house; and finds, even in winter, a light slipper or a low shoe comfortable.

The next striking peculiarity of this disorder is the flushing of the part upon exertion. This symptom, which is usually absent in the very early stage, is a notable feature of the worst of the prolonged cases, and in some mild instances can always be brought on by great exertion afoot. In the graver examples, the area of greatest pain in the soles or hands is distinctly and permanently marked by a dull, dusky, mottled redness, as if the smaller vessels were always over-distended. In these and in some of the less severe cases, the region of pain is in places tender, and firm pressure by the finger or hand will bring on increased pain, and even cause the whole foot or hand, or a part of it, to become red, just as it does when the man stands up.

Silas Weir Mitchell.

Among Mitchell's many friends were the illustrious literary personages, James Russell Lowell, Oliver Wendell Holmes, John Greenleaf Whittier and George Meredith. Mitchell died at the advanced age of eighty-four years.

An interesting but brief account of a diagnostic sign in thoracic aneurysm was contributed by William Silver Oliver (1836–1908), of Halifax, Nova Scotia, and later of various points in the British Empire. He became Surgeon General of the British Army Medical Department in 1883 after having served with varying rank since 1857. In a brief communication to the editor of the Lancet in 1878 he described his finding. The following quotation, which comprises his communication in its entirety, is from the original publication.

Physical Diagnosis of Thoracic Aneurism.

To the Editor of the Lancet

Sir:—As the diagnosis of thoracic aneurism of the aorta is often difficult and obscure, notwithstanding the various physical means we have now at our disposal for detecting it, I am desirous of mentioning a method of examination which has afforded me material assistance in diagnosing this disease (or even simple dilata-

tion of the vessel), when it occurs, as is most generally the case, either in the ascending or the first part of the transverse portion of the arch.

The process is as follows:—Place the patient in the erect position, and direct him to close his mouth, and elevate his chin to the fullest extent, then grasp the cricoid cartilage between the finger and thumb, and use gentle upward pressure on it, when if dilatation or aneurism exist, the pulsation of the aorta will be definitely felt transmitted through the trachea to the hand. The act of examination will increase the laryngeal distress should this accompany the disease.

Yours, &c.

Sept. 13, 1878 W. S. Oliver, M.D. Surgeon-Major

Important experiments dealing with the mutual relations of the heart and lungs were conducted by William Henry Welch (1850–1934), of New York and Baltimore. One of America's most celebrated pathologists and bacteriologists, he became professor of pathology at Bellevue Hospital Medical College in 1879 and at Johns Hopkins University in 1884. In 1916, he was appointed director of the School of Hygiene at the latter institution. He became professor of medical history at Johns Hopkins University in 1926.

William Henry Welch.

Welch worked with Julius Cohnheim (1839–1884) in the Institute of Pathology at Breslau and in 1878 published the results of his important experiments on the production of acute edema of the lungs. The experiments, conducted on rabbits and dogs, were performed at the suggestion of Cohnheim.

Welch stated that the frequency with which edema of the lungs was encountered at routine postmortem examination and the fact that the true nature of its production was not understood, prompted the investigation. The unanswered questions concerned the participation of hydremia or hyperemia in its pathogenesis and whether the process occurred in the arterial or in the venous tributaries. Welch concluded that edema of the lungs occurred when the outflow of blood from the left ventricle was impeded, as in failure of the ventricle. The blood, continuing to reach the lungs from the right ventricle, which was still functioning adequately, caused an increased pressure within the pulmonary circuit. This resulted in stasis and the seepage of fluid and cells into the alveoli of the lungs. The rapid occurrence of these events together with the remarkable permeability of the pulmonary capillaries favored the

ready development of pulmonary edema. These conclusions were reported in his classic article, "Zur Pathologie des Lungenödems" (1878).

Welch made many other contributions to medicine. He discovered Staphylococcus epidermidis albus and its role in wound infections in 1892, Bacillus aerogenes capsulatus (Welch bacillus) in the same year and classified the diseases resulting from it in 1900. He investigated thrombosis and embolism in 1899 and, in collaboration with Simon Flexner, demonstrated the pathologic changes resulting from the experimental injection of diphtheria toxins (1891–1892).

The first account of the disease now known as thrombo-angiitis obliterans was recorded by Felix von Winiwarter (1852–1931) of Germany. In 1879 he reported the findings in the examination of a patient with obliteration of practically all the arteries of the leg. Von Winiwarter found a chronic proliferative process which he believed was the result of a new growth of tissue from the intima of the arteries. He named the disease, "endarteritis obliterans."

Sir John Burdon Sanderson.

Pioneer studies dealing with the registration of the electrical activity of the heart were made by Sir John Burdon Sanderson (1828–1905), of England. A brilliant physiologist and teacher, a pupil of the celebrated William Sharpey (1802–1880), he was the first to record the electrical activity of the heart by means of the capillary electrometer (1880). In this work, conducted in collaboration with F. J. M. Page, he demonstrated that the electrical variations of the heart could be studied by means of Lippmann's capillary electrometer.* When zinc electrodes connected with the electrometer were applied to the back and front of the thorax, the mercury in the capillary tube moved with each beat of the heart. A record of this movement was obtained by photographing the oscillations of the column of mercury on a traveling plate. Each contraction of the heart was found to be accompanied by an electrical variation.

However, this method of registering the electrical activity of the heart was inaccurate owing to a mechanical lag in the instrument. In 1903 Willem Einthoven (1860–1927) showed that the resulting curve rep-

* Devised by Gabriel Lippmann in 1872.

resented an entirely fallacious record of the variations of the electrical potential. Nevertheless, this and future studies with this instrument were important intermediary steps in the ultimate development of electrocardiography.

An important study concerned with signs permitting the clinical diagnosis of a congenital defect of the heart was contributed by Henri-Louis Roger (1809–1891), of Paris. He served his internship at various hospitals in Paris in 1847, became a member of the Faculté de Médecine in the same year and served as physician to the Hospital for Sick Children from 1853 to 1874. Roger also served as physician to the Sèvres Street Hospital for twenty-two years, occupied a prominent position in the Association Générale des Médecins de France and was president of the Société Centrale in 1872 and of the Association Générale in 1876.

Henri-Louis Roger.

Roger's outstanding contribution to the knowledge of diseases of the heart was his description of the signs attending congenital defects of the interventricular septum. In 1861, while performing a postmortem examination on a boy, he demonstrated the presence of an interventricular septal defect unassociated with stenosis of the pulmonary artery. This observation also demonstrated that this defect alone occurs without cyanosis. Roger called attention to the presence of a thrill and the prolonged murmur so frequently present when this circumstance prevails. This characteristic murmur even today is known as the "bruit de Roger."

The following quotation in translation from Roger's classic account is noteworthy.

> . . . Its presence is revealed only by auscultation, through a physical sign with definite characteristics: this consists of a long loud *murmur* (resulting from the passage of blood through the opening in the interventricular septum and directly into the pulmonary artery or the aorta, the location of which is frequently abnormal in these cases). This murmur is unaccompanied by other murmurs, begins with systole and is so prolonged that it entirely occupies the period of the natural tic-tac of the normal heart sounds. Its point of maximal intensity is not at the apex (as in the case of lesions of the auriculo-ventricular orifice) nor at the base on the right side (as in stenosis of the aortic orifice) but over the upper third of the precordial area. It is mainly medial in location like the septum itself and from this focal point diminishes uniformly in intensity as the stethoscope is moved over the

chest. The murmur is not propagated into the vessels. It coincides with no other sign of organic disease with the exception of the *harsh thrill* which accompanies it. This murmur is *the pathognomonic sign of a defect in the interventricular septum.*

This monumental work appeared in Roger's article, "Recherches cliniques sur la communication congénitale des deux coeurs, par inocclusion du septum interventriculaire" (1879).

Supplementing the important discovery of Sir Thomas Lauder Brunton with reference to the effects of nitrites in 1867 was the therapeutic contribution of William Murrell (1853–1912), of London. Murrell received his premedical training at University College in London where he won the William Sharpey Physiological Scholarship and became demonstrator in physiology. He secured his licentiate of the Society of Apothecaries in 1874 and a year later qualified for membership in the Royal College of Surgeons. In 1877 he obtained his licentiate in the Royal College of Physicians. Murrell studied medicine at the University of Brussels and in 1879 was awarded the degree of Doctor of Medicine. In 1883 he was elected to fellowship in the Royal College of Physicians.

Pietro Burresi.

Murrell was particularly interested in the study and teaching of pharmacology, therapeutics and toxicology. His most important contribution was the introduction of nitroglycerin in the treatment of angina pectoris. The following quotation is from Murrell's classic article: "In fact, the full effect of the nitrite of amyl on the pulse is not maintained for more than fifteen seconds. The nitro-glycerine produces its effects much more slowly; they last longer and disappear gradually, the tracing not resuming its normal condition for nearly half an hour. The effect may be maintained for a much longer time by repeating the dose."

This article appeared in 1879 under the title, "Nitro-glycerine as a remedy for angina pectoris." Another work of Murrell was his "Manual of pharmacology and therapeutics," first published in 1896.

Murrell, like many other physicians, died from heart disease at the age of fifty-eight years.

Further developments in the treatment of aneurysm were introduced by the Italian surgeons, Pietro Burresi (1822–1883) and G. Corradi

(1830–1907). They applied the wiring method of Moore and Murchison (1864) and passed an electric current through the wire (1879). This method of electrocoagulation became known as the Moore-Corradi method and was employed extensively well into the twentieth century.

While previous observers had described changes in the myocardium which undoubtedly represented infarcts, their true nature was not understood.

The first exponent of the doctrine of cardiac infarction was Carl Weigert (1845–1904), of Münsterberg, Silesia, a great pathologist. His description of infarcts was clear and concise and he fully realized the relationship of the myocardial changes to obliterative changes in the coronary arteries. The account recorded by Weigert would find a proper place in any modern textbook on pathology or cardiology. The following quotation in translation is from his article, "Ueber die pathologischen Gerinnungsvorgänge," 1880.


Carl Weigert.

> With atheromatous changes of the coronary arteries thrombotic or embolic occlusions of their branches not infrequently occur. If the closures result slowly, or more important still, in such a way that collateral channels, even though insufficient for nourishment, exist there ensues a slower atrophy with disappearance of the muscle fibers, but without injury to the connective tissue. These destroyed muscle fibers are then replaced by fibrous tissue, and the so-called chronic myocarditis is nothing else but such a process.
>
> If, however, a very sudden complete cutting off of the blood supply occurs in certain parts of the heart, yellow dry masses entirely similar to coagulated fibrin result. Here, also, however, microscopic examination reveals almost no fibrous exudate, but often an apparently quite normal tissue (even the cross-striations of the muscle fibers often recognizable) but all muscle fibers and all connective tissue are devoid of nuclei. A reactive infiltration of round cells and spindle cells is present in the vicinity.

Weigert investigated the pathology of smallpox in 1874–1875 and of Bright's disease in 1879. He was the first to stain bacteria (1871) and four years later introduced the use of aniline dyes for this purpose. In 1882 he described tuberculosis of the veins and formulated the law that the degree of reparation of injured tissue exceeds the demand.

It is of considerable interest to note that a relatively obscure American physician, Frederick Winsor (1829–1889), of Massachusetts, in 1880, described angina pectoris with spontaneous rupture of the heart, and also coronary occlusion, myocardial infarction and rupture.

In the vicinity of the rent—the characteristic appearance of the muscle was lost, the muscular fibres being here filled with a granular material and in many places with minute fat drops. . . . At one point, about 3 cm. from the origin of the artery, one of these patches had so far protruded into the lumen of the vessel as to cause a coagulation of blood at that point, which coagulation had become adherent to the walls, thereby preventing the flow of blood through the vessel. The position of the heart in which the rupture had occurred and in which the fibres were found degenerated corresponded to the territory supplied by the branches of this artery.

An interesting account of traumatic valvular injuries was published by Ernest Barié (1848–1931), of France. His work was based on both clinical and experimental investigations. Barié separated traumatic lesions of the cardiac valves into two classes; namely, spontaneous rupture of the valve caused by effort on the part of the patient and trauma, whereby the injury arose from external violence. This work appeared in his article, "Recherches cliniques et expérimentales sur les ruptures valvulaires du coeur," in 1881.


Ernest Barié.

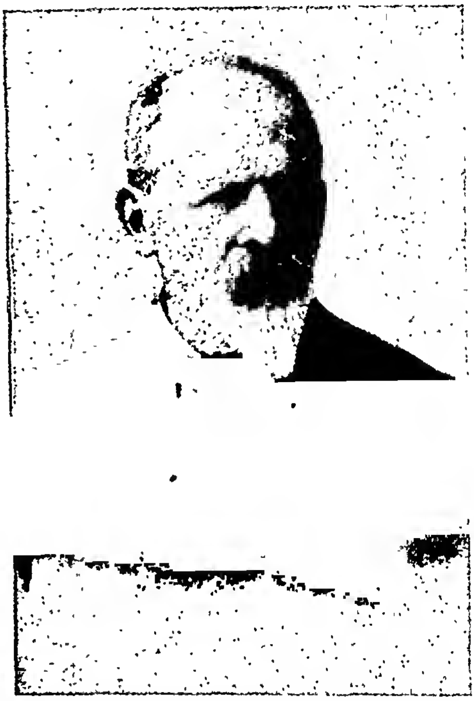
The Italian, Luigi Maria Concato (1825–1882), described the disease, polyserositis, which became known by his name. The disease is characterized by chronic inflammatory changes in the pericardium, pleura and peritoneum and at times by perihepatitis. Concato suggested a tuberculous causation of the disease. As time passed, much confusion occurred among physicians regarding Concato's disease, Pick's disease and constrictive pericarditis. Concato's article appeared under the title, "Sulla poliorromennite scrofolosa o tisi delle sierose," in 1881.

The most accurate apparatus for recording arterial blood pressure in man up to this time was devised by Ritter (Samuel Sigfried K.) von Basch (1837–1905), of Germany. The apparatus consisted of a small rubber bulb filled with water and connected with a water manometer. The bulb was applied to the radial artery and compressed until the pulse below it was completely obliterated and the pressure required to produce this effect was read off on the manometer. This work appeared in 1887 in his article, "Der Sphygmomanometer und seine Verwerthung in der Praxis."

Von Basch recorded and studied only the systolic pressure while Marey, eleven years earlier, by less precise methods had attempted to

record both the systolic and the diastolic pressures. A few years later, von Basch modified the apparatus by using a spring manometer. At about this same time Potain modified von Basch's method by using air instead of water in the bulb in union with an aneroid barometer arrangement. While these earlier studies dealing with blood pressure recordings were of definite developmental importance, great errors in actual registration occurred.

Important physiologic studies dealing with the innervation of the heart were made by the eminent English physiologist, Walter Holbrook Gaskell (1847–1914), of Cambridge. He was a student of Michael Foster and also studied under Carl Ludwig in 1874. In 1881 Gaskell produced his memorable studies on the musculature and the innervation of the heart. He demonstrated that the motor influences from the nerve ganglia in the sinus venosus affected the rhythm of the heart but did not produce the movements or the beat of the heart. These, Gaskell pointed out, were due to the autonomous rhythmic contractile power inherent in heart muscle itself and to the peristaltic contraction which proceeds from the sinus venosus to the bulbus arteriosus and from one muscle fiber to another.



Ritter (Samuel Sigfried K.) von Basch.

While working in Ludwig's laboratory, Gaskell published an article on the vasomotor nerves of striated muscle. In a later work he demonstrated the existence of two types of vasomotor nerves, both medullated and both issuing from the spinal cord by the anterior nerve roots. The vasoconstrictor nerves pass from the spinal nerves to the sympathetic nervous system by white communicating branches and return to the mixed nerve by gray communicating branches, while the vasodilating nerves accompany the spinal nerves and remain medullated until they reach the visceral ganglia. These observations appeared in his article, "On the structure, distribution and function of the nerves which innervate the visceral and vascular systems" (1885–1886).

Gaskell also produced heart block and cardiac fibrillation by experimental means and recorded early observations with the galvanometer. He also showed that the innervation of the heart is the same in both warm and cold blooded animals and that vagal stimulation depresses as well as slows the heart.

A prominent German clinician of this period, Ernst von Leyden (1832–1910), of Danzig and Berlin, aided materially in clarifying the still existent confusion regarding diseases of the coronary arteries and their relation to changes of the myocardium. He was a pupil of Johann Lucas Schönlein (1793–1864) and Ludwig Traube (1818–1876) and later succeeded the latter and Friedrich Theodor von Frerichs (1819–1885) as chief of the Berlin Clinic. Von Leyden ultimately specialized in neurology and made many important contributions to this field.

Von Leyden's most important contribution to cardiology was his article, "Ueber die Sclerose der Coronar-Arterien und die davon abhängigen Krankheitszustände," which appeared in 1884. In this work, he described four forms of coronary disease: (1) sclerosis of the coronary arteries without symptoms of cardiac impairment, (2) thrombotic obstruction of a coronary artery with acute softening and hemorrhagic infarction of the myocardium, (3) a chronic type of coronary obliteration resulting in patchy or diffuse fibrosis of the myocardium, with weakening of the ventricular wall, at times eventuating in formation of cardiac aneurysm and (4) a mixed form of chronic fibrosis associated with acute infarction of the myocardium.

Walter Holbrook Gaskell.

In an earlier publication, von Leyden had described instances of recurrent febrile episodes in patients with healed valvular lesions, which undoubtedly were instances of what is now known as subacute bacterial endocarditis.

With von Frerichs, von Leyden founded the Zeitschrift für klinische Medezin in 1879. In the field of neurology, von Leyden contributed to the knowledge of neuritis, *tabes dorsalis*, other diseases of the spinal cord and poliomyelitis.

Probably the most classic description of myocardial infarction up to this time was brought forth by Ernst Ziegler (1849–1905), professor of pathology and pathologic anatomy at the University of Freiburg. He was aware of the relationship of coronary occlusion and the resulting response of the myocardium, which he referred to as "myomalacia cordis." A brief quotation from Ziegler's work in translation is included herewith:

. . . The appearance of the softened areas varies according to their age and blood content. Shortly after the beginning of the anemia they are firm and manifest themselves only by a dull yellow coloration of the heart muscle. After some time they become soft and friable and maintain a yellowish white coloring; sometimes the cut surface sinks in somewhat, as the tissue is already softened. If the obliteration and occlusion of the arteries are followed by escape of blood from the capillaries, i.e., by hemorrhagic infarct formation, then the areas are from the beginning either dark red or dark red with brown and yellow patches, or red in the periphery and yellow in the center. . . . The areas of softening form mostly in the left ventricle, particularly the apical portion of the front or back wall. They are sometimes found in other locations, as in the wall of the right ventricle or rarely in an auricle. . . . If the softening extends to the intima, thrombi develop on the involved areas in the form of heart polyps. If the area of softening is extensive and reaches entirely or nearly through the whole muscularis, rupture of the heart wall occurs . . . when a certain stage is reached, the reparatory process starts. The detritus is absorbed and repair by cicatrix formation occurs. In the meantime round cells wander out of the vessels and a reactive inflammation occurs. The detritus is phagocyted or dissolved and absorbed and vascular granulation tissue and connective tissue form. Thus the necrotic area becomes replaced by scar tissue. . . . If the scarred area is extensive the pressure of the blood may produce an outpouching of the wall—the partial heart aneurysm.

Ernst von Leyden.

This account was published in Ziegler's "Lehrbuch der allgemeinen und speciellen pathologischen Anatomie und Pathogenese. Mit einem Anhange über die Technik der pathologisch-anatomischen Untersuchung," 1887.

A pioneer in the field of electrophysiology, Augustus Désiré Waller (1856–1922), of Paris, Edinburgh and London, made important contributions to the knowledge of the heart. Born in Paris, he was the son of an internationally known physiologist, Dr. Augustus Volney Waller (1816–1870). Young Waller graduated from the University of Aberdeen in 1878 and received the degree of Doctor of Medicine in 1881. Waller then went to London where he worked with Burdon Sanderson in his physiologic laboratory.

About 1884, Waller was appointed lecturer on physiology at the London School of Medicine for Women and, shortly thereafter, received a similar appointment in the Medical School of St. Mary's Hospital, where he taught for sixteen years. In 1902, the Senate of the University of London established a laboratory of physiology and Waller was named its director.

Waller's most important contributions to medicine were in the field of electrophysiology. He was the first to record the electrical actions of the heart in man, from the limbs. Prior to Waller's work, electrodes had been applied to the thorax but he showed that the currents could be derived from the limbs and recorded by the capillary electrometer. This demonstration was another direct step in the evolution of electrocardiography. Waller discussed these observations in the following words.

That a true electrical variation of the human heart is demonstrable may further be proved beyond a doubt by leading off from the body otherwise than from the chest wall. If the two hands or one hand and one foot be plunged into two dishes of salt solution connected with the two sides of the electrometer, the column of mercury will be seen to move at each beat of the heart, though less than when electrodes are strapped to the chest. The hand and foot act in this case as leading off electrodes from the heart and by taking simultaneous records of these movements of the mercury and of the movements of the heart it is seen that the former corresponds with the latter, slightly preceding them and not succeeding them as would be the case if they depended upon pulsation in the hand or foot.

John Alexander MacWilliam.

This observation did not find its full utilization until the relatively recent application of precordial and unipolar electrodes.

Waller's article, "A demonstration on man of electromotive changes accompanying the heart's beat," was published in 1887.

Continuing his work in electrophysiology, Waller published his account, "Signs of life from their electrical aspect," in 1903. In addition to publishing an "Introduction to human physiology" in 1891, he contributed many other articles to the current medical literature. In 1909 he delivered the Hitchcock lectures at the University of California.

An important physiologic contribution was that of John Alexander MacWilliam (1857–1937), of Aberdeen and London. In 1880 he received the degrees of Bachelor of Medicine and Master of Surgery from the University of Aberdeen and two years later, the degree of Doctor of Medicine. His graduation thesis dealt with the cardiac muscle fibers in various animals and the fibers of the diaphragm in animals. MacWilliam took graduate training at University College, London, and then worked with Carl Ludwig (1816–1895) at Leipzig. Here, together with Henry Pickering Bowditch (1840–1911), of Harvard, and Walter

Holbrook Gaskell (1847–1914), of Cambridge, he studied the physiologic properties of heart muscle. MacWilliam was thus well prepared to undertake his important physiologic studies on heart muscle.

One of MacWilliam's most outstanding works was his experiments published under the title, "Fibrillar contraction of the heart," which appeared in 1887. In these researches he demonstrated that fibrillary movements of the heart are the result of lack of harmony in the contraction and relaxation of the minute muscular fibers which compose the myocardium. MacWilliam showed that fibrillation results from "a rapid succession of incoordinated peristaltic contractions," described the relationship of the refractory period to these changes and presented evidence to the effect that certain poisons, when injected into the blood stream, result in fibrillation of the ventricles. He held the belief that sudden death during chloroform anesthesia is attributable to ventricular fibrillation.

Étienne-Louis-Arthur Fallot.

In 1913 MacWilliam contributed a paper, "Blood pressures in man in normal and pathologic conditions," which was published in "Heart."

In 1888, Graham Steell (1851–1942), of Manchester, described the diastolic murmur of pulmonary regurgitation which at times accompanies the increased intrapulmonary pressure associated with mitral stenosis. When Willius and Keys sought biographic data from Dr. Steell at the time of preparation of their "Cardiac classics" he permitted the reproduction of his original article but requested that no biographic comments be included. The senior author therefore still accedes to this request.

The following quotation from Steell's article well summarizes the main theme of his interesting and instructive article. "I wish to plead for the admission among the recognized auscultatory signs of disease of a *murmur due to pulmonary regurgitation, such regurgitation occurring independently of disease or deformity of the valves, and as the result of long-continued excess of blood pressure in the pulmonary artery.*" Still today, this murmur is known as the Graham Steell murmur.

Particularly interested in congenital malformations of the heart, Étienne-Louis-Arthur Fallot (1850–1911), of Marseille, presented the most comprehensive account of "maladie bleue." He studied medicine

at the École de Médecine at Marseille and following graduation served as substitute professor of medicine at the University of Marseille from 1882 to 1886. In 1886 Fallot taught pathologic anatomy and in 1888 was appointed professor of hygiene and legal medicine, which post he held until his death.

Fallot's important work appeared under the title, "Contribution à l'anatomie pathologique de la maladie bleue (cyanose cardiaque)," in 1888. The ensuing quotation, in translation, partly records his conclusions.

> This malformation consists of a true anatomopathologic type represented by the following tetralogy: (1) Stenosis of the pulmonary artery; (2) Interventricular communications; (3) Deviation of the origin of the aorta to the right; (4) Hypertrophy, almost always concentric, of the right ventricle. Failure of obliteration of the foramen ovale may occasionally be added in a wholly accessory manner.

John S. Bristowe.

Instances of this combination of congenital anomalies had previously been recorded by Sandifort (1777), William Hunter (1784), Farre (1814), Gintrac (1824) and Peacock (1866) but did not attract the attention that was accorded Fallot's classic account. Even today, the condition is referred to as the tetralogy of Fallot.

A splendid account of paroxysmal tachycardia was published by John S. Bristowe (1827–1893), of London. His article, "On recurrent palpitations of extreme rapidity in persons otherwise apparently healthy," appeared in 1888. Bristowe commented on the intermittent character of the disorder, its relative frequency, its sudden onset and abrupt termination, and its occurrence in patients with apparently normal hearts. The following brief quotations are from Bristowe's article.

> . . . That hearts may beat with the extreme rapidity with which I have found them to beat, is a fact which, I think, has been largely overlooked, and with which I, at any rate, had no practical acquaintance until within the last two or three years; and yet I feel sure, judging from my recent experience, that the condition which I am about to discuss is of frequent occurrence, and needs only to be looked for intelligently to be recognized in many persons who are regarded as merely nervous and liable to attacks of ordinary palpitation. . . .
>
> . . . The patient was a fairly healthy-looking young married lady, who had evidently been liable for some years to attacks of palpitation, and was free from structural disease of the heart. The attack in which I saw her came on suddenly,

without apparent cause, and after a week left her as suddenly as it had arisen. Her pulse varied between 180 and 192 in a minute. A few weeks later she had a recurrence of palpitation, when the cardiac beats were counted at 246. What seemed to me at the time the most remarkable feature of her case was the apparent absence of distress. . . .

It is to be remembered that Cotton had reported on a case of extremely rapid heart action in 1867, but his description lacked the classic features of paroxysmal tachycardia other than the rapidity of the cardiac rate.

A year after Bristowe's description, Leon Bouveret (1850–1929), of Lyon, named this rapid disorder of the heart, *tachycardie essentielle paroxystique* (essential paroxysmal tachycardia). A graduate of Paris, he became the leading consultant of Lyon.

Henri Huchard.

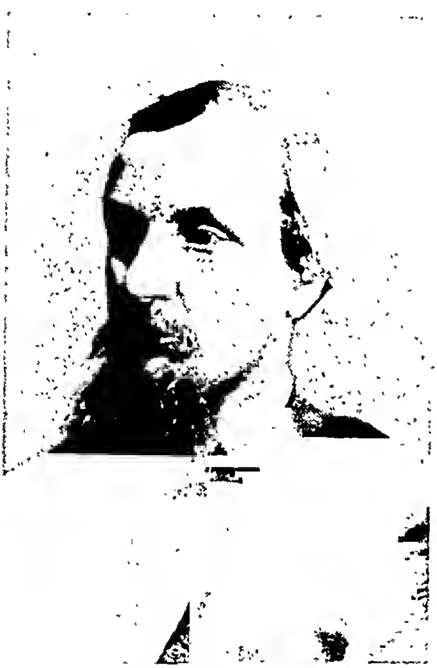
Bouveret's observations were published in his article, "De la tachycardie essentielle paroxystique," in 1889. He emphasized the paroxysmal character of the disorder, the extreme regularity of the rapid pulse, the absence of evidence of heart disease and the abrupt onset and sudden termination of the attack. Bouveret considered the possibilities that the disorder might indicate paralysis of the vagus nerve, a mediastinal tumor pressing on the vagus, or a bulbar lesion. However, when the paroxysm subsided and examination still revealed normal findings, he relinquished these speculations and concluded correctly that a neurogenic factor of functional character was responsible for the rapid heart action.

Another prominent French clinician, Henri Huchard (1844–1910), of Auxon (Aube), made contributions to cardiology. His most prominent work, "Traité des maladies du coeur et des vaisseaux, artériosclérose, aortites, cardiopathies arterielles, angines de poitrine," Paris, was published in 1889.

Huchard discussed the variable clinical phenomena of coronary disease and considered spasm of the coronary arteries to be one of a number of causes of angina pectoris. He also investigated heart block and suggested that it might be the result of arteriosclerosis of the cerebral arteries, particularly those of the medulla. It was Huchard who suggested that heart block be called "Adams-Stokes disease."

Important contributions dealing with the peripheral vascular system were made by Sir Jonathan Hutchinson (1828–1913), of Selby, Yorkshire, and London. He was a graduate of St. Bartholomew's Hospital and became surgeon to the London Hospital from 1859 to 1883, and professor of surgery at the Royal College of Surgeons from 1879 to 1883. Hutchinson was an able surgical pathologist, kept meticulous case records and notes and went to great lengths to obtain postmortem data.

Hutchinson was the first to describe temporal arteritis and his account was published in 1890 under the title "On a peculiar form of thrombotic arteritis of the aged which is sometimes productive of gangrene. (With plate.)" He introduced the subject by discussing thrombophlebitis of superficial and deep veins, drawing a parallelism between these lesions and the subject to be considered. The following quotations are of interest:



Sir Jonathan Hutchinson.

> . . . My object in the present paper is to ask attention to certain facts which seem to suggest that the arteries are liable to a parallel form of disease—one, namely, in which there is a spreading plastic inflammation which glues the artery to its sheath, and at the same time produces thrombotic plugging of the vessel, to be followed by permanent obliteration. This form of arteritis occurs, I believe, most often in elderly persons, or, at any rate, in those past middle life; probably it never happens to arteries which are perfectly sound. I do not, however, feel in the least sure that the advanced calcareous degeneration of old age is a frequent predisponent. In the case which is the principal subject of the present paper, although the patient was advanced in years and the arteries not sound, yet they were not calcareous. There is no proof, nor, I think, much probability, that anything of the nature of embolic plugging precedes this condition of thrombotic arteritis. It is very difficult indeed to say what its initial stage is, and I may remark that it is equally so in the case of thrombotic phlebitis. . . . The disease which has been named arteritis obliterans is, I believe, usually one of somewhat slow progress, and is not supposed to be accompanied by thrombosis, whereas the condition to which I now wish to draw attention is one of rapid development, and has for its principal feature thrombotic occlusion of the vessel implicated. . . .

Hutchinson then interrupts the presentation of the case under discussion (in which the patient was a woman seventy-four years of age with gangrene of the left leg requiring amputation), to recall a patient he had observed many years ago on whom he had made the diagnosis of temporal arteritis.

. . . He was upwards of eighty, and almost in his dotage. I was asked to see him because as I was told, he had red "streaks on his head" which were painful and prevented his wearing his hat. As I have said, he was bald, and his scalp was thin. The "red streaks" proved, on examination, to be his temporal arteries, which on both sides were found to be inflamed and swollen. The streaks extended from the temporal region almost to the middle of the scalp, and several branches of each artery could be distinctly traced. The conditions were nearly symmetrical. During the first week that he was under my observation pulsation could be feebly detected in the affected vessels, but it finally ceased; the redness then subsided, and the vessels were left impervious cords. At no time was any gangrene of the skin of the scalp threatened. The old gentleman lived, I believe, several years after this without any other manifestation of arterial disease. . . .

Hutchinson wrote on Raynaud's disease and was the first to call attention to the confusion that existed in the medical literature regarding this disease. He also wrote extensively on diseases of the skin. Hutchinson described the serrated, peg-shaped incisor teeth of congenital syphilis in 1861 (Hutchinson's teeth) and varicella gangrenosa in 1882 and he expressed the belief that leprosy resulted from eating fish. He also contributed to the field of neurology.

Scipione Riva-Rocci.

In 1889, Hutchinson established the "Archives of Surgery" to which he was the sole contributor. The first volume appeared in 1890 and ten volumes completed the publication. Interesting plates in color accompanied many of the articles.

Further perfection of the sphygmomanometer resulted from the genius of Scipione Riva-Rocci (1863–1937), the brilliant Italian physiologist. He developed the mercury sphygmomanometer, which, in principle, was the model for those in present-day use. He used an inflated rubber bag to obliterate the pulse in the brachial artery and recorded the pressure necessary to obtain this effect in millimeters at the level of the mercury contained in the tube of the manometer at the instant that the pulse in the radial artery disappeared.

Riva-Rocci's investigations were well developed in 1891 but not published until later. His article, "Un nuovo sfigmomanometro," was published in 1896. This work represented the true origin of modern determinations of blood pressure.

One of the first articles dealing with the medicolegal aspects of sudden death with special reference to coronary disease was published by Ludwig Hektoen (1863–), of Chicago. For many years he was

professor of pathology at the University of Chicago and one of America's outstanding pathologists. His article, "Embolism of left coronary artery: sudden death," was published in 1892. Hektoen insisted that the coronary arteries should be carefully examined in all cases of sudden death in which medicolegal problems were existent.

A pioneer in the histologic study of the cardiac conduction system was Wilhelm His, Jr. (1863–1934), of Leipzig and Berlin. Born in Basel, Switzerland, he became a German subject in 1895. His father was professor of anatomy at the University of Basel and later at the University of Leipzig. The younger His graduated from the University of Leipzig in 1888 and a year later became Heinrich Curschmann's (1846–1910) assistant at Leipzig.


Wilhelm His, Jr.

In 1891, His became associate professor of internal medicine at the University of Leipzig, taught at Dresden in 1901, a year later succeeded Friedrich Müller at Basel and in 1907 accepted the post vacated by Ernst von Leyden at Berlin.

During the time that His was associated with Curschmann, he contributed to a volume, "Arbeiten aus dem medizinischen Klinik zu Leipzig" (1893), which contained his findings on the histology of the junctional region of the heart. He believed that he had demonstrated a bundle of specialized tissue bridging the auricles and ventricles, the A-V bundle or bundle of His. Even though the existence of a specific anatomic structure has been questioned there can be no doubt regarding the presence of a functional conducting pathway. The title of His's article was "Die Thätigkeit des embryonalen Herzens und deren Bedeutung für die Lehre von der Herzbewegung beim Erwachsenen," 1893. The following brief quotation in translation is from this work.

> . . . After extensive investigation I was able to find a muscle bundle which connects the auricular and ventricular septal walls, and which apparently had not been observed before, because it is only visible in its entire distribution when the septal walls are cut exactly in the horizontal direction.

A year before His's death he summarized the events leading up to his discovery in the following words.

It was the current teaching of the time that the ganglia are the autonomic centers of the heart. Only Engelmann, in Utrecht, and Gaskell, in Cambridge, held the belief, based on their experiments, that the heart muscle itself is able to originate rhythmic stimuli. I was present one day when Krehl and Romberg discussed these subjects. I proposed to them to study from an embryological point of view the development of the heart to try to ascertain whether or not the heart is able to beat before it has nerves and ganglia. At that time I had finished an embryological paper under my father's direction and was, therefore, familiar with the technique necessary for such a study.

I followed the development of the cardio-nervous system through several vertebrates and could prove that in all these animals the heart beats before it receives cerebral spinal nerves or ganglia. One point remained mysterious, namely, the conduction of the stimulus from one part of the heart to the other.

Gaskell had shown that in the frog and turtle the conduction is made by way of the muscles. I tried to prove such a muscular connection in the adult mammal and in human beings by examining serial sections in the various embryonic stages. I finally found these muscular connections and described them in 1893. Few have read this paper.

Other important studies dealing with cardiac conduction were made by A. F. Stanley Kent (1863–), of England. After years of patient investigation he demonstrated the existence of accessory muscular connections between the right auricle and ventricle in various animals. Kent conducted extensive histologic studies of the auriculoventricular groove of the hearts of animals. His studies indicated that these accessory communications were most abundant in the hearts of young animals and in creatures low in the scale of animal life. As the age of the animal increased and the scale of animal development rose, the accessory connections became fewer and were less well developed. Kent demonstrated that while such communications were present in the hearts of monkeys, the most highly developed animal studied, they were fewer than in other species.

From 1893 to 1914 Kent published eight papers pertaining to his investigations. The first two appeared in 1893; the others after a lapse of twenty years. The second publication was titled "Researches on the structure and function of the mammalian heart."

While Kent's work was generally known (the accessory communication became known as the "bundle of Kent") it was not universally accepted until after 1932, when his publications were reviewed critically and verified by the investigations of Holzman and Scherf, Wolferth and Wood, and Wood, Wolferth and Geckeler.

One of the greatest discoveries of all times was that of Wilhelm Konrad Roentgen (1845–1922) (see special biography), who variously was professor of physics at Strasbourg, Giessen, Würzburg and Munich. His discovery of the x-rays affected every branch of medicine profoundly. Roentgenography and roentgenoscopy have been of inestimable value in the more precise diagnosis of diseases of the heart and aorta.

Shortly after Roentgen's discovery, he communicated his findings at a meeting of the Würzburg Physico-Medical Society on December 28,

1895. This report was published in his classic article, "Ueber eine neue Art von Strahlen," 1895.

In 1895, the introduction of the purine drugs occurred when S. Askanazy (1866–), of Germany, produced theobromine sodiosalicylate (diuretin). This preparation was first recommended as a diuretic and the original article appeared under the title, "Klinisches über Diuretin." This work marked the admission of the purines into the treatment of cardiac and renal diseases. Since then a large number of closely allied preparations have been successively introduced. The value of the purine derivatives in the treatment of the anginal syndrome is still a debatable subject.

William Ewart.

Discussing the signs of pericardial effusion, William Ewart (1848–1929), of London, described an area of percussion dullness which he believed was pathognomonic of the condition. He was physician to St. George's Hospital and to the Belgrave Hospital for Children. Ewart published his article, "Practical aids in the diagnosis of pericardial effusion, in connection with the question as to surgical treatment," in 1896. He discussed twelve signs of pericardial effusion and the eighth sign is still today known as Ewart's sign. The following quotation is from his article.

The Posterior Pericardial Patch of Dulness.—Whenever fluid is effused into the pericardium the normal resonance is modified at the left posterior base in a most definite way. A patch of marked dulness is found at the left inner base, extending from the spine for varying distances outward, usually not quite so far as the scapular (angle) line, and ceasing abruptly with a vertical outer boundary. Above, its extension is also variable, according to the size of the effusion; commonly it does not extend higher than the level of the ninth or tenth rib, and here again its horizontal boundary is abrupt. Its shape then is that of a square, and it is quite unlike that of any dulness arising from pleuritic effusion. You will not experience any difficulty in identifying the patch in question. Rather greater care in percussion is needed, however, to follow the dulness as it extends to the corresponding vertebrae, and for a short distance also to the right of them. For some time I had overlooked this extension, which, owing to the general resonance of the right base is one of partial dulness only. When, however, the effusion is considerable, the extension of the patch in the right chest may become almost absolutely dull. . . . The value of this sign is that, unlike many others, it is very sharply defined, and does not fit any other diagnosis.

The first case of coronary thrombosis diagnosed during the life of the patient in the United States was recorded by George Dock (1860–). An outstanding clinician and teacher, he variously served as professor of medicine at the University of Texas in Galveston (1889–1891), University of Michigan (1891–1908), Tulane Medical School (1908–1910) and Washington University of St. Louis (1910–1922).

In 1896, while at the University of Michigan, Dock reported the case of a thirty-six year old man in whom the diagnosis of occlusion of the right coronary artery was confirmed by postmortem examination. This account was published as "Some notes on the coronary arteries."

An important physiologic investigation dealing with the experimental ligation of the coronary arteries was conducted by William Townsend Porter (1862–), professor of comparative physiology at Harvard Medical School. Following coronary ligation, Porter noted that the procedure frequently resulted in fibrillary contractions of the heart and sudden death. However, death did not always occur and this led him to conclude that Cohnheim's (1881) consistently fatal results were due to operative trauma and that the coronary arteries were not end arteries. Porter's work appeared in 1894 under the title, "On the results of ligation of the coronary arteries."

George Dock.

Five years later, Porter's student, Walter Baumgartner, in the same laboratory, repeated the experiments and produced infarcts of the myocardium. Baumgartner's work was published as "Infarction of the heart" in 1899.

An unusual clinical syndrome with involvement of the pericardium was described by Friedel Pick (1867–1926) while working in Pribram's clinic at Prague. He had observed three cases of this peculiar syndrome in which postmortem examination had been conducted and in which pseudocirrhosis of the liver was present associated with chronic adhesive pericarditis involving the mediastinum. No marked clinical evidence of cardiac involvement had been present and no evidence of venous stasis occurred in the upper portions of the body in spite of the presence of considerable ascites. The hepatic changes did not conform to those seen in cases of primary cirrhosis but resembled a mixed form of cirrhosis with ascites but without jaundice. Pick stated that the

changes in the liver resulted from the disturbances of circulation caused by the obliterative mediastinopericarditis. The disturbances of circulation resulted in an increase of the connective tissue of the liver which produced stasis in the portal system eventuating in ascites.

Pick called attention to the frequency of this disease in young patients but emphasized the point that the disease also occurred later in life. He suggested the possibility that tuberculosis might be the causative agent. This work appeared in 1896 in his article, "Über chronische, unter dem Bilde der Lebercirrhose verlaufende Pericarditis (pericarditische Pseudolebercirrhose) nebst Bemerkungen über die Zuckergussleber (Curschmann)." This syndrome has continued to be called "Pick's disease."

The undesirability of attaching the name of the discoverer of a disease to the disease is clearly demonstrated in the case of Pick's disease. In addition to the disease described by Friedel Pick two other diseases bearing the same name occur in medical literature and medical dictionaries. Circumscribed atrophy of the brain associated with progressive degeneration of the higher faculties together with aphasia was described by Arnold Pick and is frequently referred to as Pick's disease. Also, erythromelalgia described by Filipp Josef Pick is known as Pick's disease. Misunderstanding and confusion are the ready outgrowth of the regrettable custom of eponymic naming of a disease.

Another accurate account of cardiac infarction was recorded by René Marie (1868–   ), of Paris. He contended that, when a coronary artery of considerable size becomes occluded by a thrombus (not by an embolus), infarction of the myocardium results. The artery which becomes occluded is usually sclerotic. Marie called attention to the fact that the appearance of the myocardium differs according to the time of examination from the moment of the vascular stoppage. He then described the various changes of tissue ranging from the anemic stage to disintegration of muscle and hyaline changes. This work appeared in 1896 in his publication, "L'infarctus du myocarde," Paris.

One of the earliest accounts concerned with the use of the x-rays in the diagnosis of diseases of the heart and aorta was that of Francis Henry Williams (1852–1936) (see special biography), of Boston. A graduate of the Massachusetts Institute of Technology in 1873, he later attended Harvard Medical School, from which institution he received the degree of Doctor of Medicine in 1877. Williams established practice in Boston and, less than a year after Roentgen's monumental discovery, published his first article on the subject, which appeared under the title, "A method for more fully determining the outline of the heart by means of the fluoroscope together with other uses of this instrument in medicine" (1896).

By means of the roentgenoscope, Williams demonstrated enlargement of the heart, thoracic aneurysm, pericardial effusion, transposition of

the heart, emphysema, pleuritis with effusion, pneumothorax, hydro-pneumothorax and pulmonary tuberculosis. The importance of Roentgen's discovery and of the contributions of Williams and the many succeeding roentgenologists to medicine and to cardiology is fully appreciated by modern physicians.

Prior to the attempt of Guido Farina, the eminent Italian surgeon, to suture a penetrating wound of the heart no attempts except that of C. J. B. Williams, reported in 1835, had been made to save the lives of such patients. While Farina's attempt to suture a wound in the right ventricle did not save this particular patient, his courage and the procedure employed clearly opened the way for the future development of surgery of the heart. He showed that suture of wounds of the heart is possible and the passage of the years has verified the feasibility of surgical intervention.

Ballance published an interesting private letter from Farina to Sir John Bland-Sutton, written in December, 1909, which merits reproduction here.

> The first case of surgical interference on the heart which I had the opportunity of performing was carried out in March, 1896, at the Spedala della Consolazione. The patient was a man 30 years of age, who received a blow from a very fine and sharp dagger in the fifth intercostal space in the parasternal line. The wound penetrated to the cavity in an oblique direction from above downwards, and from without inwards. It wounded the pericardium and penetrated into the ventricle. The wound in the myocardium was about 7 mm. long. I removed the fifth costal cartilage and a bit of the rib for about 15 cm. Then I strongly retracted the fourth and sixth costal cartilages. I arrived on the wounded heart. I sutured the wound with three silk sutures, and between these particular points I placed two others of less importance. Everything went well till the fifth day, when a violent broncho-pneumonia declared itself on the right side and in three days killed the patient. The thoracic wound healed by primary intention.
>
> At the autopsy the wound in the heart was found to be perfectly healed. The heart was not allowed to be preserved for further study. It was precisely because of my irritation at this fact that I have not published any communication on this interesting case.

While the exact reasons why this heart was not allowed to be preserved are not stated, one is still confounded by the obstacles to scientific research displayed so late in the nineteenth century. This is truly reminiscent of the Dark Ages. At the same time one cannot fail to admire the reticence on the part of an individual who had been unjustifiably frustrated simply because he did not choose to demonstrate an unprecedented and successful achievement to his colleagues without the material evidence.

Another early case of stab wound of the heart, inflicted by means of a table knife, was recorded by Louis Rehn (1849–1930), of Frankfurt am Main. On the day following the injury, at which time bleeding of the wound continued and signs of pericardial distention were present, Rehn opened the thorax. He evacuated blood clots from the pericardium and

pleural cavity and sutured the wound in the heart and pericardium. The patient recovered.

Rehn performed the operation in 1896 but did not publish his report until 1907, at which time the patient was still alive.

Descriptions of physical signs pertaining to the diagnosis of diseases of the pericardium continued to appear toward the close of the century. Such a contribution was recorded by Sir William Henry Broadbent (1835–1907), of Manchester and London. He received the degree of Bachelor of Medicine from the University of London in 1856 and the degree of Doctor of Medicine from the same institution four years later. In 1861 Broadbent became a member of the Royal College of Physicians. He was a student of Francis Gibson and from this great teacher derived his special interest in diseases of the thorax.

Sir William Henry Broadbent.

In addition to being an excellent clinician, Broadbent was a neurologist and obstetrician of note. He described the systolic retraction of the left intercostal spaces as a sign of adherent pericarditis, which is still referred to as "Broadbent's sign." Because of the fact that some modern clinicians have misinterpreted Broadbent's account of this physical sign, probably because they have not read his original description, the following quotation is offered.

Systolic retraction of the lower portions of the posterior or lateral walls of the thorax may indicate the presence of a universally adherent pericardium. Such retraction may, however, be seen though the pericardium is not adherent to the heart, but only to a larger extent than normal to the central tendon of the diaphragm and the muscular substance on either side and to the chest wall as well. In such cases the heart is usually greatly enlarged and hypertrophied from old valvular disease. The explanation seems to be that the portion of the diaphragm to which the pericardium is adherent is dragged upwards at each systole of the heart, so that the points of attachment of the digitations of the diaphragm to the lower ribs and costal cartilages are dragged inwards and retracted.

Broadbent published this work in collaboration with his son, Sir John F. H. Broadbent (died 1946), in the book, "Heart disease; with special reference to prognosis and treatment," 1897.

In 1884, Broadbent delivered a series of lectures before the Harveian Society on prognosis in valvular disease of the heart and three years later presented the Croonian lectures on the pulse before the Royal College

of Physicians. In 1891 he delivered the Lumleian lectures, in which he discussed the prognosis in structural diseases of the heart. The material from the lectures formed the basis of the text of Broadbent's book.

A rare combination of congenital anomalies was reported by V. Eisenmenger, of Germany. He described an arrangement similar to that seen in the tetralogy of Fallot (the tetralogy of Fallot consists of a defect of the interventricular septum, stenosis of the pulmonary artery, dextroposition of the aorta and hypertrophy of the right ventricle) but instead of the pulmonary artery being narrowed, the pulmonary artery or valve is normal in size or dilated. This set of anomalies has since been known as "Eisenmenger's complex."

Eisenmenger's article appeared in 1897 under the title, "Die angeborenen Defecte der Kammerscheidewand des Herzens."

We have repeatedly referred to the prevailing confusion regarding coronary disease in the second half of the nineteenth century in spite of certain concise and accurate studies. In the last years of this century, Karl Dehio (1851–1927), of Dorpat, Russia, published an article which was greatly at variance with the concepts which were gradually being evolved. He believed that when a patient died without cardiac failure, myocardial fibrosis was only minimal in degree, but that when failure with exhaustion of the heart and subsequent cardiac dilatation was present the fibrous myocardial changes were marked and extensive. Dehio attributed the myofibrosis to increased viscosity of the blood.

As already shown, the work of Callender, Farina and Rehn had demonstrated the feasibility of surgical intervention on the heart. In 1898, Edmond Delorme (1847–1929), of Paris, professor of surgery at the Val-de-Grâce, who previously had been the first to perform decortication of the lungs in chronic empyema, recommended the same procedure in cases of adherent pericarditis. He published his article, "Sur un traitement chirurgical de la symphyse cardopéricardique," in 1898 before he had performed the operation. The following is a quotation from P. D. White's translation.

> If the surgeon feels legitimate regrets in publishing a method of treatment which he has conceived but been unable as yet to apply, on the other hand he risks the loss of advantage of the original idea and the compromise of its application if he waits too long. It is to avoid this last difficulty that I have resolved to speak to you of a surgical treatment of cardio-pericardial adhesions concerning which I deposited a confidential note in 1895 at the Academy of Medicine and the application of which I have been unable to effect, despite repeated appeals to my colleagues of the medical services of the Val-de-Grâce Hospital. This treatment consists of the resection or destruction of the cardio-pericardial adhesions.

SUMMARY

The second half of the nineteenth century was indisputably the greatest era of medical progress yet encountered. All branches of medical science shared in this progress and notable were the achievements

attained in the field of the heart and circulation. The existent freedom of thought and expression created limitless frontiers for scientific exploration.

Tremendous progress became evident in physiology through the talents, investigations and teachings of such brilliant physiologists as Bernard, Foster, Gaskell, Fick, Bowditch, Sanderson, Marey, von Basch, Riva-Rocci and others. The creation of new instruments of greater precision and the graphic and quantitative measurement of results opened an entirely new approach to the study of body functions.

Closely correlated with this physiologic approach to unknown problems were the monumental studies in electrophysiology, which each in correlating sequence established the groundwork for the ultimate development of the electrocardiograph and electrocardiography. Based on earlier discoveries, the researches of Kölliker and Müller, Waller and MacWilliam placed this work on a remarkably clear basis.

Researchers in the field of pathology secured new and important information regarding many diseases of the heart and circulation. Among these workers were Kirkes, Virchow, Winge, Wilks, Heiberg, Rokitansky, Cohnheim, Welch and Ziegler, to mention only a few.

A long line of illustrious clinicians and teachers contributed generously and significantly to the establishment of more precise diagnostic procedures for the recognition of disease. Among them were Duroziez, Flint, Potain, Quincke, DaCosta, Traube, Gull and Sutton, Kussmaul, Gowers, von Leyden, Steell and Huchard.

Significant contributions with regard to congenital anomalies of the heart and their clinical recognition were found in the works of Peacock, Roger, Fallot and Eisenmenger.

The two great therapeutic innovations were those of Brunton and Murrell.

Surgery of the heart and arteries came into being and, while still limited, nevertheless unmistakably demonstrated the possibilities of this new field of surgery. The pioneers in this field included Broca, Moore, Murchison, Callender, Burresi, Corradi, Farina, Rehn and Delorme.

Without a doubt one of the greatest discoveries of this era was that of Roentgen. The discovery of the x-rays and their utilization as a precise diagnostic method completely revolutionized the recognition of disease.

The essential pattern of modern medical education became established through the precepts and experience of a long line of illustrious teachers. Didactic instruction combined with bedside demonstration and laboratory training, particularly in the basic medical sciences, offered the greatest opportunities yet afforded to medical students. American medicine came of age in this period and many medical col-

leges became established. Some were excellent in their teaching and facilities while many others were literally upstarts which did not survive. As educational standards were raised and the reputation of the truly great schools became established, many of the smaller colleges ceased to exist or were absorbed by ranking schools.

In spite of the remarkable progress that was achieved in regard to the heart and circulation, certain diseases of the heart remained confused and controversial issues. This was the case with so-called chronic myocarditis, which existed as a vague entity and conveniently served as a diagnostic category for various forms of cardiac disease which did not fit the then accepted orthodox clinical picture. Thus, many instances of coronary disease, hypertensive heart disease, the heart in hyperthyroidism, and certain cases of chronic pericarditis, were grouped under the general caption of chronic myocarditis. Virchow's great influence continued to prevail and even well into the first quarter of the twentieth century, chronic myocarditis served as a convenient term for uncertain diagnoses.

Even though numerous workers had attempted to clarify the problem of coronary disease, great differences of opinion prevailed. No general concept of gradual or abrupt closure of coronary arteries and their clinical manifestations existed. The myofibrosis of ischemia was still considered as chronic myocarditis. The relationship of angina pectoris to coronary sclerosis remained a controversial issue and many causes were assigned to this symptom complex. In order to illustrate this latter point a widely acclaimed textbook, published in 1898, namely, the well-written work of George Alexander Gibson (1854–1913), of Edinburgh, "Diseases of the heart and aorta," contained the following comments regarding angina pectoris: "The group of symptoms known, from the date of their earliest scientific analysis, by the term angina pectoris, forms a variable picture, produced by morbid conditions scarcely if at all, less diverse in character than the clinical appearances."

REFERENCES

Quain

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, pp. 425 and 667.

Gibson, G. A.: Diseases of the heart and aorta. New York, The Macmillan Company, 1898, pp. 652, 663, 720 and 744.

Herrick, J. B.: A short history of cardiology. Springfield, Illinois, Charles C Thomas, 1942, pp. 215–217.

Willius, F. A.: Cardiac clinics. CXV. The historic development of knowledge relating to the coronary circulation and its diseases: the nineteenth century. Proc. Staff Meet., Mayo Clin. 21:82 (Feb. 20) 1946.

Bernard

Castiglioni, Arturo: A history of medicine. (Translated by E. B. Krumbhaar.) New York, Alfred A. Knopf, 1941, pp. 682–683.
Garrison, F. H.: Op. cit., pp. 544–547.
White, P. D.: Heart disease. Ed. 3, New York, The Macmillan Company, 1944, p. 958.

Kirkes

Garrison, F. H.: Op. cit., p. 569.
Gibson, G. A.: Op. cit., pp. 390 and 402.
Herrick, J. B.: Op. cit., pp. 176–178.
*Kirkes, W. S.: On some of the principal effects resulting from the detachment of fibrinous deposits from the interior of the heart, and their mixture with the circulating blood. Tr. Med.-Chir. Soc. London, 35:281–324, 1852.
Major, R. H.: Classic descriptions of disease; with biographical sketches of the authors. Ed. 2, Springfield, Illinois, Charles C Thomas, 1939, pp. 502–503.
Obituary: William Senhouse Kirkes, M.D., F.R.C.P. Lancet. 2:674 (Dec. 10) 1864.
Power, D'Arcy: William Senhouse Kirkes, M.D. St. Barth. Hosp. J. 18:166–168, 1910–1911.
Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors. St. Louis, C. V. Mosby Company, 1941, pp. 471–482.

Stannius

Garrison, F. H.: Op. cit., p. 558.
White, P. D.: Op. cit., p. 958.

Broca

Broca, P.-P.: Des anévrysmes et de leur traitement. Paris, Labé, 1856, 931 pp.
Castiglioni, Arturo: Op. cit., p. 715.
Garrison, F. H.: Op. cit., pp. 492–493.
Matas, Rudolph: Personal experiences in vascular surgery; statistical synopsis. Ann. Surg. 112:811–812 (Nov.) 1940.

Vierordt

Castiglioni, Arturo: Op. cit., p. 682.
Garrison, F. H.: Op. cit., p. 558.

Bidder

Garrison, F. H.: Op. cit., pp. 541, 548, 558 and 691.

Hyrtl

Garrison, F. H.: Op. cit., pp. 462–464.
Gibson, G. A.: Op. cit., p. 67.
Gross, Louis: The blood supply to the heart; in its anatomical and clinical aspects. New York, Paul B. Hoeber, 1921, p. 79.
Willius, F. A.: Op. cit., p. 86.

Virchow

Castiglioni, Arturo: Op. cit., pp. 695–698.
Garrison, F. H.: Op. cit., pp. 569–572.
Herrick, J. B.: Op. cit., pp. 166–170.
Major, R. H.: Op. cit., pp. 552–557.
White, P. D.: Op. cit., p. 958.
Willius, F. A.: Op. cit., p. 83.

Kölliker

Garrison, F. H.: Op. cit., pp. 461–462.
Hirschfelder, A. D.: Diseases of the heart and aorta. Ed. 3, Philadelphia, J. B. Lippincott Company, 1918, p. 82.
*von Kölliker, R. A. and Müller, Heinrich: Nachweis der negativen Schwankung des Muskelstroms am natürlich sich contrahirenden Muskel. Verhandl. d. phys.-med. Gesellsch. 6:528–533, 1856.
White, P. D.: Op. cit., p. 171.

Foster

Castiglioni, Arturo: Op. cit., pp. 788–789.
Garrison, F. H.: Op. cit., pp. 558–559.
Gibson, G. A.: Op. cit., p. 60.
White, P. D.: Op. cit., p. 959.

Malmsten

Benson, R. L.: General review: The present status of coronary arterial disease. Arch. Path. & Lab. Med. 2:879–880 (Dec.) 1926.
Castiglioni, Arturo: Op. cit., p. 834.
Garrison, F. H.: Op. cit., p. 704.
Willius, F. A.: Op. cit., pp. 82–83.

Duroziez

*Duroziez, P.: Du double souffle intermittent crural, comme signe de l'insuffissance aortique. Arch. gén. de méd. 107:417–443 (Apr.); 588–605 (May) 1861.
Gibson, G. A.: Op. cit.,pp. 297, 501 and 502.
Helfenbein, Fciga: Duroziez et son oeuvre; contribution à l'histoire de la cardiologie. Thesis, Paris, 1922, No. 430, 36 pp.
Major, R. H.: Op. cit., pp. 397–398.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 491–496.

Flint

Carpenter, W. M.: III.—Memoir of Austin Flint, M. D., LL. D. Tr. M. Soc. New York. 81:556–565, 1887.
Castiglioni, Arturo: Op. cit., pp. 825–826.
*Flint, Austin: On cardiac murmurs. Am. J. M. Sc. 44:29–54 (July) 1862.
Garrison, F. H.: Op. cit., p. 632.
Gibson, G. A.: Op. cit., pp. 497, 499, 500 and 534.
Herrick, J. B.: Op. cit., p. 104.
Landis, H. R. M.: Austin Flint: his contributions to the art of physical diagnosis and the study of tuberculosis. Bull. Johns Hopkins Hosp. 23:182–186 (June) 1912.
Major, R. H.: Op. cit., pp. 390–393.
Necrology: Austin Flint, Sr., M. D., LL. D. J.A.M.A. 6:361–364 (Mar. 27) 1886.
Walsh, J. J.: History of medicine in New York, three centuries of medical progress. New York, National Americana Society, Inc., 1919, vol. 4, pp. 14–15.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 497–528.

Trousseau

Ballance, Charles: Bradshaw lecture on the surgery of the heart. Lancet. 1:73 (Jan. 10) 1920.
Garrison, F. H.: Op. cit., p. 616.

Panum

Castiglioni, Arturo: Op. cit., pp. 925–926.
Garrison, F. H.: Op. cit., p. 574.
Gibson, G. A.: Op. cit., p. 68.
Gross, Louis: Op. cit., p. 79.
*Panum, P. L.: Experimentelle Beiträge zur Lehre von der Embolie. Virchows Arch. f. path. Anat. 25:308–338, 1862.
Willius, F. A.: Op. cit., p. 86.

Raynaud

Garrison, F. H.: Op. cit., pp. 296, 645 and 666.
*Raynaud, A.-G.-M.: De l'asphyxie locale et de la gangrène symétrique des extrémités. Paris, Rignoux, 1862, 177 pp.

Lancereaux

Castiglioni, Arturo: Op. cit., pp. 784 and 829.
Gibson, G. A.: Op. cit., pp. 247, 249, 381, 680 and 767.
Willius, F. A.: Op. cit., p. 80.

Moore and Murchison

*Moore, C. H. and Murchison, Charles: On a new method of procuring consolidation of fibrin in certain incurable aneurisms. Tr. Med.-Chir. Soc. London. 47:129–149, 1864.

Peacock

Garrison, F. H.: Op. cit., pp. 433 and 574.
Gibson, G. A.: Op. cit., p. 228.
Hirschfelder, A. D.: Op. cit., p. 534.
*Peacock, T. B.: 9. Partial rupture of the aorta and separation of the coats by the extravasated blood; "dissecting aneurysm." Tr. Path. Soc. London. 25:59–61, 1874.
White, P. D.: Op. cit., p. 959.

Brunton

*Brunton, T. L.: On the use of nitrite of amyl in angina pectoris. Lancet. 2:97–98 (July 27) 1867.
Castiglioni, Arturo: Op. cit., p. 898.
Garrison, F. H.: Op. cit., pp. 653–654.
Garrison, F. H.: Sir Thomas Lauder Brunton, M. D. (1844–1916); an apostle of preparedness. Mil. Surgeon. 40:369–377 (Apr.) 1917.
Gibson, G. A.: Op. cit., pp. 248, 249 and 276.
Obituary: Sir Lauder Brunton, Bt., M. D., F. R. S., consulting physician to St. Bartholomew's Hospital, London. Brit. M. J. 2:440–442 (Sept. 23) 1916.
Obituary: Sir T. Lauder Brunton, Bart., M. D., C. M., D. Sc. Edin., M. D. R. U. I. (Hon.), LL. D. Edin. and Aberd. (Hon.), F. R. C. P. Lond., F. R. S., consulting physician to St. Bartholomew's Hospital. Lancet. 2:572–575 (Sept. 23) 1916.
Power, D'Arcy: In memoriam: Sir Thomas Lauder Brunton, F. R. S., 1844–1916. St. Barth. Hosp. Rep. 52:1–9, 1916.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 557–564.

Cotton

*Cotton, R. P.: Notes and observations upon a case of unusually rapid action of the heart (232 per minute). Brit. M. J. 1:629–630 (June 1) 1867.
Gibson, G. A.: Op. cit., p. 802.
Major, R. H.: Op. cit., pp. 432–435.

Nothnagel

Allbutt, Clifford: Diseases of the arteries including angina pectoris. London, Macmillan and Co., Limited, 1915, vol. 2, p. 351.
Castiglioni, Arturo: Op. cit., p. 820.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 622–623.
Gibson, G. A.: Op. cit., pp. 247, 249, 773 and 804.
Hirschfelder, A. D.: Op. cit., p. 387.
°Schwalbe, J.: Hermann Nothnagels letzte Niederschrift: Bemerkungen über seine stenokardischen Anfälle. Deutsche med. Wchnschr. 2:1564–1565 (Sept. 28) 1905.
Willius, F. A.: Op. cit., p. 80.

Potain

Castiglioni, Arturo: Op. cit., p. 828.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 636.
Gibson, G. A.: Op. cit., p. 827.
°Potain, P. C. E.: Des mouvements et des bruits qui se passent dans les veines jugulaires. Bull. et mém. Soc. méd. d. hôp. de Paris. s. 2, 4:3–27, 1867.
°Potain, M.: Théorie du bruit de galop. Compt. rend. Assoc. française pour l'avancement d. sci. (pt. 1) 1885, pp. 201–203.
Vaquez, M. H.: Pierre-Carl Potain (1825–1901): Éloge prononcé a l'académie de médecine dans la séance annuelle du 13 Decembre 1927. Bull. Acad. de méd., Paris. s. 3, 98:569–587, 1927.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 529–556, 651–652.

Quincke

Annotations: Heinrich Quincke. Lancet. 1:1259 (June 24) 1922.
von Bergmann, G.: Heinrich Quincke. Gedenkrede bei einer Trauerfeier der medizinischen Fakultät und des ärztlichen Vereins zu Frankfurt am Main. Ztschr. f. klin. Med. 96:1–21 (Sept. 22) 1923.
Castiglioni, Arturo: Op. cit., p. 889.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 642.
Gibson, G. A.: Op. cit., pp. 493, 814 and 840.
Hochhaus, H.: Heinrich Quincke zum 70. Geburtstag. Deutsche med. Wchnschr. 2:1605–1607 (Aug. 22) 1912.
Hoppe-Seyler, G.: Heinrich Quincke. München. med. Wchnschr. 2:1014–1016 (July 7) 1922.
Külbs: Heinrich Quincke. Deutsches Arch. f. klin. Med. 140:I–IV, 1922.
Major, R. H.: Op. cit., pp. 681–683.
°Quincke, H.: II. Beobachtungen über Capillar- und Venenpuls. Berl. klin. Wchnschr. 5:357–359 (Aug. 24) 1868.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 565–573.

Winge

Gibson, G. A.: Op. cit., p. 390.
Herrick, J. B.: Op. cit., pp. 178–179.
°Winge, E. F. H.: Endocarditis hos en man, som vårdades för pyemi. Förh. Svens. Läk. Sällsk. Sammank, Stockholm. 32:172–175, 1870.

Wilks

Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 628–629.
Gibson, G. A.: Op. cit., p. 681.
Herrick, J. B.: Op. cit., p. 203.
Major, R. H.: Op. cit., pp. 507–512.

White, W. H.: Samuel Wilks. Guy's Hosp. Rep. s. 3, 52:2–39, 1913.
*Wilks, Samuel: Capillary embolism or arterial pyaemia. Guy's Hosp. Rep. s. 3, 15:29–35, 1870.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 575–584.

Fick

*Fick, A.: Eine Verbesserung des Blutwellenzeichners. Arch. f. d. ges. Physiol. 30:597–601, 1883.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 535 and 686.
Gibson, G. A.: Op. cit., pp. 59, 175, 723 and 739.
White, P. D.: Op. cit., p. 959.

Bowditch

*Bowditch, H. P.: Über die Eigenthümlichkeiten der Reizbarkeit, welche die Muskelfasern des Herzens zeigen. Arb. a. d. Physiol. Anat. zu Leipzig (1871). *6:139–176, 1872.*
*Bowditch, H. P.: Note on the nature of nerve-force. J. Physiol. 6: 133–135, 1885.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 537–538.
Hirschfelder, A. D.: Op. cit., pp. 1 and 21.

DaCosta

Castiglioni, Arturo: Op. cit., p. 824.
*DaCosta, J. M.: On irritable heart; a clinical study of a form of functional cardiac disorder and its consequences. Am. J. M. Sc. *61:17–52* (Jan.) 1871.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 633 and 760.
Gibson, G. A.: Op. cit., p. 735.
Herrick, J. B.: Op. cit., p. 104.
White, P. D.: Op. cit., pp. 515–517.

Traube

Boruttau, H.: Ludwig Traube und die Geschichte der experimentellen Pathologie in Deutschland. (Kritische Bemerkungen.) Ztschr. f. exper. Path. u. Therap. 20:144–148, 1919.
Castiglioni, Arturo: Op. cit., p. 820.
Correspondence: The death of Louis Traube. M. Rec. 11:323–324 (May 13) 1876.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 621.
Gibson, G. A.: Op. cit., pp. 218 and 730.
Haberling, W.: Zum hundertsten Geburtstag Ludwig Traubes. Deutsches med. Wchnschr. 1:21–23 (Jan. 3) 1918.
Herrick, J. B.: Op. cit., p. 107.
von Leyden, E.: Gedächtnissrede auf Ludwig Traube. Charité-Ann. 2:767–800, 1877.
Major, R. H.: Op. cit., pp. 417–419.
Morrison, Hyman: Ludwig Traube. Boston M. & S. J. 196:1097–1101 (June 20) 1927.
*Traube, L.: Ein Fall von Pulsus bigeminus nebst Bemerkungen über die Leberschwellungen bei Klappenfehlern und über acute Leberatrophie. Berl. klin. Wchnschr. 9:185–188 (Apr. 15); 221–224 (May 6) 1872.
Virchow, Rud.: Zur Erinnerung an L. Traube. Berl. klin. Wchnschr. 13:209–210 (Apr. 17) 1876.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 585–599.

Heiberg

Biographische Mittheilungen: Hjalmar Heiberg. Leopoldina. 4:39–40, 1898.
*Heiberg, Hjalmar: Ein Fall von Endocarditis ulcerosa puerperalis mit Pilzenbildungen im Herzen (Mycosis endocardii). Arch. f. path. Anat. 56:407–414, 1872.

Gull

Castiglioni, Arturo: Op. cit., p. 821.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 627–628.
Gibson, G. A.: Op. cit., p. 730.
*Gull, W. W. and Sutton, H. G.: On the pathology of the morbid state commonly called chronic Bright's disease with contracted kidney ("arteriocapillary fibrosis"). Tr. Med.-Chir. Soc. London. 55:273–326, 1872.
Herrick, J. B.: Op. cit., p. 196.
White, P. D.: Op. cit., p. 959.

Moxon and Durham

*Moxon, W. and Durham, A. E.: Case of abdominal aneurism cured by compression of the aorta. Tr. Med.-Chir. Soc. London. 55:213–224, 1872.

Kussmaul

Bast, T. H.: The life and time of Adolf Kussmaul. Ann. M. Hist. 8:95–127, 1926.
Castiglioni, Arturo: Op. cit., p. 820.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 621–622.
Gibson, G. A.: Op. cit., pp. 327, 360 and 366.
*Kussmaul, A.: Ueber schwielige Mediastino-Pericarditis und den paradoxen Puls. Berl. klin. Wchnschr. 10:433–435 (Sept. 15); 445–449 (Sept. 22); 461–464 (Sept. 29) 1873.
Major, R. H.: Op. cit., pp. 259–262.
Widenmann, A.: Quoted by Hirschfelder, A. D., op. cit., p. 621.

Callender

*Callender, G. W.: Removal of a needle from the heart. Recovery of the patient. Tr. Med.-Chir. Soc. London. 56:203–212, 1873.

Fagge

Benson, R. L.: Op. cit., p. 879.
*Fagge, C. H.: 11. A series of cases of fibroid disease of the heart. Tr. Path. Soc. London. 25:64–98, 1874.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 629.
Gibson, G. A.: Op. cit., p. 859.
Willius, F. A.: Op. cit., p. 83.

Francis H. Welch

Gibson, G. A.: Op. cit., pp. 370, 823 and 830.
Herrick, J. B.: Op. cit., p. 204.
* Welch, F. H.: On aortic aneurism in the army, and the conditions associated with it. Tr. Med.-Chir. Soc. London. 59:59–77, 1876.
White, P. D.: Op. cit., p. 959.

Rokitansky

Castiglioni, Arturo: Op. cit., pp. 694–695.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 432–433.

Gibson, G. A.: Op. cit., pp. 285, 291 and 645.
*Rokitansky, Carl: Die Defekte der Scheidewände des Herzens. Pathologische-anatomische Abhandlung. Wien, W. Braumüller, 1875, 156 pp.
White, P. D.: Op. cit., p. 959.

Gowers

Castiglioni, Arturo: Op. cit., p. 890.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 643.
Langdon, F. W.: Sir W. R. Gowers, M.D., F.R.C.P., F.R.S.; an appreciation. Lancet-Clinic. 114:142–144, 1915.
Obituary: Sir William Gowers, M.D., F.R.C.P., F.R.S., consulting physician to University College Hospital and to the National Hospital for the Paralysed and Epileptic, London. Brit. M. J. 1:828–830 (May 8) 1915.
Obituary: Sir William Richard Gowers, M.D. Lond. and Dub., F.R.C.P. Lond., LL.D. Edin., F.R.S., consulting physician to University College Hospital, London, and to the National Hospital for the Paralysed and Epileptic, Queen-Square, W.C. Lancet. 1:1055–1056 (May 15) 1915.
Obituary: Sir William Richard Gowers, M.D., F.R.C.P., F.R.S. Boston M. & S. J. 172:877–878 (June 10) 1915.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 601–611.

Marey

Castiglioni, Arturo: Op. cit., pp. 683–684.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 535 and 558.
Willius, F. A. and Keys, T. E.: Op. cit., p. 532.

Cohnheim

Benson, R. L.: Op. cit., p. 881.
* Cohnheim, Julius: The pathology of the circulation. Thrombosis and embolism. In: Lectures on general pathology. A handbook for practitioners and students. (Translated by Alexander B. McKee.) London, The New Sydenham Society, 1889, sect. I, chap. 4, pp. 172–241.
*Cohnheim, Jul. and von Schulthess-Rechberg, Ant.: Ueber die Folgen der Kranzarterienverschliessung für das Herz. Virchows Arch. f. path. Anat. 85: 503–536, 1881.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 572–573.
Gibson, G. A.: Op. cit., pp. 69, 105, 232, 337, 627 and 737.
Gross, Louis: Op. cit., p. 80.
Willius, F. A.: Op. cit., pp. 86–87.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 613–619.

Gairdner

Gibson, G. A.: Op. cit., pp. 769 and 775.
Willius, F A.: Op. cit., p. 80.

Southey

Bryant, Thomas: President's address: Reginald Southey, M.D. Oxon., F.R.C.P. Lond. Tr. Med.-Chir. Soc. London. 83:cxx–cxxi, 1900.
Gibson, G. A.: Op. cit., p. 264.
*Southey, R.: Traitement de l'anasarque general par un drainage capillaire. Compt. rend. Assoc. française pour l'advancement d. sci. 1877, p. 857; also quoted by White, P. D., op. cit., p. 788.
White, P. D.: Op. cit., p. 959.

Hammer

°Hammer, Adam: Ein Fall von thrombotischem Verschlusse einer der Kranzarterien des Herzens. Am Krankenbette konstatirt. Wien. med. Wchnschr. 28:97–102, 1878; also quoted by Major, R. H., op. cit., pp. 398–402.
Major, R. H.: Op. cit., pp. 462–467.
Willius, F. A.: Op. cit., p. 83.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 10 and 816.

Rotch

Castiglioni, Arturo: Op. cit., p. 859.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 635.
Gibson, G. A.: Op. cit., p. 338.
Herrick, J. B.: Op. cit., p. 187.
Major, R. H.: Op. cit., pp. 444–446.
°Rotch, T. M.: Absence of resonance in the fifth right intercostal space diagnostic of pericardial effusion. Boston M. & S. J. 99:389–393 (Sept. 26); 421–429 (Oct. 3) 1878.

S. Weir Mitchell

Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 644–645.
Major, R. H.: Op. cit., pp. 522–526.
°Mitchell, S. W.: Article I. On a rare vaso-motor neurosis of the extremities, and on the maladies with which it may be confounded. Am. J. M. Sc. 76:17–36 (July) 1878.

Oliver

Gibson, G. A.: Op. cit., p. 344.
Major, R. H.: Op. cit., pp. 501–502.
°Oliver, W. S.: Physical diagnosis of thoracic aneurism. Lancet. 2:406 (Sept. 21) 1878.

W. H. Welch

Castiglioni, Arturo: Op. cit., pp. 816–817.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 586.
°Welch, W. H.: Zur Pathologie des Lungenödems. Arch. f. path. Anat. u. Physiol. 72:375–412 (Mar. 5) 1878.

von Winiwarter

von Winiwarter, F.: Quoted by Buerger, Leo: Thrombo-angiitis obliterans: a study of the vascular lesions leading to presenile spontaneous gangrene. Am. J. M. Sc. 136:567–580 (Oct.) 1908.

Sanderson

Castiglioni, Arturo: Op. cit., p. 789.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 687.
Gibson, G. A.: Op. cit., p. 64.
°Sanderson, J. and Page, F. J. M.: On the time-relations of the excitatory process in the ventricle of the heart of the frog. J. Physiol. 2:384–435, 1880.
White, P. D.: Op. cit., p. 959.
Willius, F. A. and Keys, T. E.: Op. cit., p. 720.

Roger

Castiglioni, Arturo: Op. cit., p. 858.
Lereboullet, P.: Henri Roger (1809–1891). Paris méd. 14:25, 1914.
Obituary: Henri Roger. Mém. et bull. Soc. de méd. et chir. de Bordeaux (1892). 1893, pp. 5–6.

°Roger, Henri: Recherches cliniques sur la communication congénitale des deux coeurs, par inocclusion du septum interventriculaire. Bull. Acad. de méd., Paris. s. 2, 8:1074–1094; 1189, 1879.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 621–636.

Murrell

Gibson, G. A.: Op. cit., p. 781.
°Murrell, William: Nitro-glycerine as a remedy for angina pectoris. Lancet. 1: 80–81 (Jan. 18); 113–115 (Jan. 25); 151–152 (Feb. 1); 225–227 (Feb. 15) 1879.
Obituary: William Murrell, M.D., Brux., F.R.C.P. Lond., senior physician to, and lecturer on medicine at, Westminster Hospital. Lancet. 2:124 (July 13) 1912.
Spencer, W. G.: In memoriam: William Murrell, M.D., F.R.C.P. Westminst. Hosp. Rep. (1911–1912). 18:11–15, 1913.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 639–650.

Burresi and Corradi

Burresi, P. and Corradi, G.: Lo Sperimentale. 43:445, 1879; also quoted by King, E. S. J.: Surgery of the heart. Baltimore, Williams & Wilkins Company, 1941, p. 702.

Weigert

Benson, R. L.: Op. cit., pp. 880–881.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 573–574.
Herrick, J. B.: Op. cit., pp. 220–222.
°Weigert, Carl: Ueber die pathologischen Gerinnungsvorgänge. Arch. f. path. Anat. u. Physiol. 79:87–123 (Jan. 15) 1880.
Willius, F. A.: Op. cit., p. 84.

Winsor

Benson, R. L.: Op. cit., p. 880.
Willius, F. A.: Op. cit., p. 83.
°Winsor, Frederick: Angina pectoris with rupture of the heart. Quoted by Putney, G. E.: Extracts from the records of the Middlesex East District Medical Society. Boston M. & S. J. 103:398–400 (Oct. 21) 1880.

Barié

°Barié, E.: Recherches cliniques et expérimentales sur les ruptures valvulaires du coeur. Rev. de méd., Paris. 1:132–144, 1881.
Gibson, G. A.: Op. cit., pp. 447–448.
White, P. D.: Op. cit., p. 959.

Concato

Concato, L.: Sulla poliorromennite scrofolosa o tisi delle sierose. Giorn. internaz. d. Sc. med. 3:1037, 1881; also quoted by White, P. D., op. cit., p. 668.
White, P. D.: Op. cit., p. 658.

von Basch

°von Basch, S.: II. Der Sphygmomanometer und seine Verwerthung in der Praxis. Berl. klin. Wchnschr. 24:179–183 (Mar. 14) 1887.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 636.
Gibson, G. A.: Op. cit., p. 194.
White, P. D.: Op. cit., p. 959.

Gaskell

Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 558 and 560–561.
*Gaskell, W. H.: On the structure, distribution and function of the nerves which innervate the visceral and vascular systems. J. Physiol. 7:1–80, 1885.
Gibson, G. A.: Op. cit., p. 87.
White, P. D.: Op. cit., p. 959.

von Leyden

Benson, R. L.: Op. cit., p. 881.
Castiglioni, Arturo: Op. cit., p. 820.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 622.
Herrick, J. B.: Op. cit., pp. 181 and 223.
*Leyden, E.: Ueber die Sclerose der Coronar-Arterien und die davon abhängigen Krankheitszustände. Ztschr. f. klin. Med. 7:459–486; 539–580, 1884.
Willius, F. A.: Op. cit., p. 84.

Ziegler

Gibson, G. A.: Op. cit., pp. 680, 684 and 686.
Herrick, J. B.: Op. cit., p. 223.
Willius, F. A.: Op. cit., pp. 84–85.
*Ziegler, Ernst: Lehrbuch der allgemeinen und speciellen pathologischen Anatomie und Pathogenese. Mit einem Anhange über die Technik der pathologisch-anatomischen Untersuchung. Jena, G. Fischer, 1887, vols. 1 and 2, 499 pp. and 1020 pp.
*Ziegler, Ernst: General pathology. (Translated by A. S. Warthin.) New York, William Wood and Company, 1908, pp. 163–165.

Waller

Castiglioni, Arturo: Op. cit., pp. 782, 787 and 794.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 569 and 657.
Gibson, G. A.: Op. cit., pp. 64 and 65.
Obituary: Augustus D. Waller, M.D., LL.D., F.R.S., director of the physiological laboratory of the University of London. Brit. M. J. 1:458–459 (Mar. 18) 1922.
Obituary: Augustus Désiré Waller, M.D., C.M. Aberd., D.Sc. Perth, W.A., Hon. LL.D. Edin., Hon. M.D. Geneva, F.R.S.; director of the physiological laboratory, University of London, Lancet. 1:555 (Mar. 18) 1922.
*Waller, A. D.: A demonstration on man of electromotive changes accompanying the heart's beat. J. Physiol. 8:229–234, 1887.

MacWilliam

Cruickshank, E. W. H.: Prof. J. A. MacWilliam, F.R.S. Nature. 139:224–225 (Feb. 6) 1937.
*MacWilliam, J. A.: Fibrillar contraction of the heart. J. Physiol. 8:296–310, 1887.
Obituary: John Alexander MacWilliam, M.D., LL.D. Aberd., F.R.S. Lancet. 1: 236–237 (Jan. 23) 1937.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 679–685.

Steell

*Steell, Graham: The murmur of high-pressure in the pulmonary artery. Med. Chron., Manchester. 9:182–188, 1888–1889.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 679–685.

Fallot

°Fallot, A.: Contribution à l'anatomie pathologique de la maladie bleue (cyanose cardiaque). Marseille med. 25:77; 138; 207; 270; 341; 403, 1888.
Gibson, G. A.: Op. cit., p. 305.
Olmer, D.: "Étienne-Louis Arthur Fallot" in Leçon d'ouverture de la chaire de clinique médicale. Marseille méd. 66:741–759, 1929.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 687–690.

Bristowe

°Bristowe, J. S.: On recurrent palpitation of extreme rapidity in persons otherwise apparently healthy. Brain. 10:164–198 (July) 1888.
Gibson, G. A.: Op. cit., p. 802.
White, P. D.: Op. cit., p. 864.

Bouveret

°Bouveret, L.: De la tachycardie essentielle paroxystique. Rev. de méd., Paris. 9:753–793, 1889.
Gibson, G. A.: Op. cit., p. 802.
Major, R. H.: Op. cit., pp. 436–438.

Huchard

Benson, R. L.: Op. cit., p. 876.
Castiglioni, Arturo: Op. cit., p. 829.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 618.
Gibson, G. A.: Op. cit., pp. 249, 757, 808, 809 and 811.
Herrick, J. B.: Op. cit., pp. 195–196.
Willius, F. A.: Op. cit., p. 82.

Hutchinson

Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 597.
°Hutchinson, Jonathan: Diseases of the arteries. Arch. Surg., Lond. 1:323, 1889–1890.

Riva-Rocci

Castiglioni, Arturo: Op. cit., p. 832.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 636.
Hirschfelder, A. D.: Op. cit., pp. 27–28.
White, P. D.: Op. cit., p. 959.

Hektoen

Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 787.
°Hektoen, Ludvig: Embolism of left coronary artery: sudden death. M. News. 61: 210–212 (Aug. 20) 1892.
Herrick, J. B.: Op. cit., p. 226.

His, Jr.

Blech, G. M.: Obituary; Dr. Wilhelm His. Mil. Surgeon. 76:99 (Feb.) 1935.
Castiglioni, Arturo: Op. cit., pp. 781 and 782.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 530 and 686.
Gibson, G. A.: Op. cit., pp. 5, 6, 7 and 61.
°His, Wilhelm, Jr.: *Die Thätigkeit des embryonalen Herzens und deren Bedeutung für die Lehre von der Herzbewegung beim Erwachsenen.* Arch. a. d. med. Klin. zu Leipzig. 1893, pp. 14–49.

°His, Wilhelm: Zur Geschichte des Atrioventrikularbündels nebst Bemerkungen über die embryonale Herztätigkeit. Klin. Wchnschr. 12:569–574 (Apr. 15) 1933.
In Memoriam: Wilhelm His. Klin. Wchnschr. 13:1689–1692 (Nov. 24) 1934.
von Krehl, L.: Wilhelm His. München med. Wchnschr. 2:2044–2045 (Dec. 29) 1933.
Obituary: Wilhelm His: Jun. Lancet. 2:1200 (Nov. 24) 1934.
Schilling, V.: Wilhelm His; (geboren 29. 12. 63, gestorben 10. 10. 34). Deutsches Arch. f. klin. Med. 177:I–VIII (Dec.) 1934.
Staehelin, R.: Wilhelm His zum siebzigsten Geburtstage. Klin. Wchnschr. 12: 1995–1996 (Dec.) 1933.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 691–695.

Kent

Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 686–687.
Hirschfelder, A. D.: Op. cit., p. 568.
Holzmann, Max and Scherf, D.: Über Elektrokardiogramme mit verkürzter Vorhof-Kammer-Distanz und positiven P-Zacken. Ztschr. f. klin. Med. 121:404–423, 1932.
°Kent, A. F. S.: Researches on the structure and function of the mammalian heart. J. Physiol., 14:233–254, 1893.
°Kent, A. F. S.: Observations on the auriculo-ventricular junction of the mammalian heart. Quart. J. Exper. Physiol. 7:193–195, 1913.
°Kent, A. F. S.: The structure of the cardiac tissues at the auriculo-ventricular junction. J. Physiol. 47:xvii–xix, 1913.
°Kent, A. F. S.: The right lateral auriculo-ventricular junction of the heart. J. Physiol. 48:xxii–xxiv, 1914.
°Kent, A. F. S.: A conducting path between the right auricle and the external wall of the right ventricle in the heart of a mammal. J. Physiol. 48:lvii, 1914.
°Kent, A. F. S.: Illustrations of the right lateral auriculo-ventricular junction in the heart. J. Physiol. 48:lxiii–lxiv, 1914.
Wolferth, C. C. and Wood, F. C.: Further observations on the mechanism of the production of a short P-R interval in association with prolongation of the QRS complex. Am. Heart J. 22:450–457 (Oct.) 1941.
Wood, F. C., Wolferth, C. C. and Geckeler, G. D.: Histologic demonstration of accessory muscular connections between auricle and ventricle in a case of short P-R interval and prolonged QRS complex. Am. Heart J. 25:454–462 (Apr.) 1943.

Roentgen

Castiglioni, Arturo: Op. cit., pp. 772 and 907.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 721–722.
Hirsch, I. S.: Editorial. Wilhelm Conrad Roentgen; his life and work. Radiology. 4:63–66 (Jan.); 139–142 (Feb.); 249–253 (Mar.) 1925.
°Röntgen, W. C.: Ueber eine neue Art von Strahlen. Sitzungsb. d. phys.-med. Gesellsch. zu Würzburg. 1895, pp. 132–141.

Askanazy

°Askanazy, S.: Klinisches über Diuretin. Deutsches Arch. f. klin. Med. 56:209–230 (Dec.) 1895.
Willius, F. A.: Op. cit., p. 88.
Willius, F. A.: Some historical notes on the treatment of angina pectoris. Minnesota Med. 19:415–421 (July) 1936.

Ewart

°Ewart, William: Practical aids in the diagnosis of pericardial effusion, in connection with the question as to surgical treatment. Brit. M. J. 1:717–721 (Mar. 21) 1896.

Gibson, G. A. : Op. cit., pp. 172 and 339.
Herrick, J. B.: Op. cit., p. 187.
Hirschfelder, A. D.: Op. cit., p. 600.

Dock

Dock, George: Some notes on the coronary arteries. M. & S. Reporter. 75:1–7, 1896.
Herrick, J. B.: Op. cit., p. 213.
Major, R. H.: Op. cit., pp. 467–470.
Willius, F. A.: Op. cit. (Cardiac clinics. CXV), p. 85.

Porter

°Baumgarten, W.: Infarction of the heart. Am. J. Physiol. 2:243–265 (Mar. 1) 1899.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), pp. 563 and 791.
Hirschfelder, A. D.: Op. cit., p. 378.
°Porter, W. T.: On the results of ligation of the coronary arteries. J. Physiol. 15:121–138, 1894.
White, P. D.: Op. cit., p. 959.
Willius, F. A.: Op. cit. (Cardiac clinics, CXV), p. 87.

Pick

Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 636.
Herrick, J. B.: Op. cit., p. 189.
Hirschfelder, A. D.: Op. cit., p. 619.
°Pick, Friedel: Über chronische, unter dem Bilde der Lebercirrhose verlaufende Pericarditis (pericarditische Pseudolebercirrhose) nebst Bemerkungen über die Zuckergussleber (Curschmann). Ztschr. f. klin. Med. 29:385–410, 1896.
White, P. D.: Op. cit., pp. 658–659.

Marie

Gibson, G. A.: Op. cit., pp. 685–686.
Herrick, J. B.: Op. cit., p. 219.
Marie, R.: L'infarctus du myocarde. Paris; also quoted by Gibson, G. A., op. cit., pp. 685–686.
White, P. D.: Op. cit., p. 959.

F. H. Williams

Brown, Percy: American martyrs to science through the roentgen rays. Springfield, Illinois, Charles C Thomas, 1936, 276 pp.
Brown, Percy: Francis Henry Williams, 1852–1936. (Editorial.) Am. J. Roentgenol. 36:106–110 (July) 1936.
°Williams, F. H. A method for more fully determining the outline of the heart by means of the fluoroscope together with other uses of this instrument in medicine. Boston M. & S. J. 135:335–337 (Oct. 1) 1896.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 697–706.

Farina

Ballance, Charles: Op. cit., p. 4.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 596.
Matas, Rudolph: Surgery of the vascular system. In Keen, W. W.: Surgery; its principles and practice by various authors. Philadelphia, W. B. Saunders Company, 1909, vol. 5, p. 41.

Rehn

Ballance, Charles: Op. cit., p. 4.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 596.
Matas, Rudolph: Op. cit. (Surgery of the vascular system), p. 41.

Broadbent

*Broadbent, W. H. and Broadbent, J. F. H.: Heart disease; with special reference to prognosis and treatment. Ed. 3, New York, William Wood & Co., 1900, 420 pp.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 646.
Gibson, G. A.: Op. cit., p. 360.
Leaders in modern medicine: VII.—Sir William H. Broadbent, Bart. Practitioner. (Aug.) 1908, pp. 329–335.
Major, R. H.: Op. cit., pp. 447–452.
Obituary: Sir William Henry Broadbent, Bart., K. C. V. O., M. D. Lond., F. R. C. P. Lond., LL. D. Edin. & St. And. & Toronto, D. Sc. Leeds, F. R. S.; Commander of the Legion of Honour; physician in ordinary to H. M. the King and H. R. H. the Prince of Wales, consulting physician to St. Mary's Hospital, the London Fever Hospital, and the New Hospital for Women. Lancet. 2:126–130 (July 13) 1907.
Obituary: Sir William Henry Broadbent, Bart., K. C. V. O., M. D. Lond., F. R. C. P., F. R. S., Hon. LL. D. Edin., St. And., and Toronto, Hon. D. Sc. Leeds; physician in ordinary to the King and to the Prince of Wales; consulting physician to St. Mary's Hospital. Brit. M. J. 2:177–181 (July 20) 1907.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 707–715.

Eisenmenger

*Eisenmenger, Victor: Die angeborenen Defecte der Kammerscheidewand des Herzens. Ztschr. f. klin. Med. 32(Suppl.):1–28 (Feb. 5) 1897.

Dehio

Dehio, Karl: Myofibrosis cordis. Deutsches Arch. f. klin. Med. 62:1–62 (Dec.) 1898.
Willius, F. A.: Op. cit. (Cardiac clinics. CXV), p. 86.

Delorme

Castiglioni, Arturo: Op. cit., p. 849.
Delorme: Sur un traitement chirurgical de la symphyse cardo-péricardique. Bull. et mém. Soc. de chir. de Paris. n.s. 24:918–922, 1898.
Garrison, F. H.: Op. cit. (An introduction to the history of medicine), p. 596.
White, P. D.: Op. cit., p. 666.

* Indicates original source consulted by the authors.

8

THE FIRST QUARTER OF THE TWENTIETH CENTURY

*"The keynote of progress in the twentieth century is system and organization,—in other words, 'team-work.'"**

THE AMAZING progress in medicine and its integrated sciences, which has already occurred in the twentieth century and which is destined to occur in the remaining years of the century, is largely based on the contributions of the previous eras of civilization. The preceding half century, as already emphasized, was truly a golden age of medicine, and so well were the fundamental principles in all branches of medical science defined that nothing short of a cosmic cataclysm could prevent almost limitless future progress and development.

As already stated earlier in this volume, no attempt will be made to record events beyond the first quarter of the century. The progress achieved in the field of cardiovascular diseases since 1925 is tremendous and must be reserved for the attention of subsequent authors. At the present time, nearly half the century already has been traversed and it is not reckless to predict that the contributions to come will be still more amazing and spectacular. As in the preceding centuries, great physicians lived to extend their influence from one era into the next while a new generation of illustrious physicians succeeded them. Many of these distinguished names are fresh in the memories of present-day physicians, and the newcomers, especially in the United States, comprise our friends and contemporaries. Many noteworthy contributors among them are living and continuing to exert their influence in the history of medicine and it will be the privilege of some future compilers of historical data to include them in a later contribution.

The first quarter of the twentieth century, like previous eras, was temporarily disturbed by war, epidemics and economic upheaval. World War I brought both devastation and reward. Through necessity, numerous important medical discoveries occurred which became applied to civilian medicine when peace was again restored.

Early and important articles dealing with the cerebral effects of digitalis were those of Harry Orville Hall of Washington, D. C. While Duroziez, as early as 1874, had reported a series of cases of delirium occurring during the therapeutic administration of digitalis and current textbooks made mere mention of such mental derangements, the articles

* Charles H. Mayo (1865–1939). Journal-Lancet, 36:1–3, 1916.

of Hall did much to bring the problem before the profession. Hall's first article on this subject appeared in 1901 under the title, "The hallucinations of digitalis; does digitalis cause hallucinations, delirium or insanity under certain conditions?" The following quotation from this article is of interest.

> It is possible that only in rare instances has this effect been noticed or been attributed, if noticed, to the use of digitalis, and yet is it not also possible that where delirium or hallucinations have occurred in connection with the administration of digitalis, these symptoms have been attributed to the disease from which the patient was suffering, and not to the medicine prescribed? In other words, are the symptoms which manifest themselves during treatment always attributed to the right cause? May they not frequently arise from the medication employed and not from the disease? . . .

Hall then described an instance of the cerebral effects of digitalis intoxication.

> . . . It ran along in the usual course for several weeks, and then it began to be reported that the patient was "out of her mind" at times. At these times she would have strange hallucinations. For example, she would say to the nurse, "I am now going to die," and then she would compose her limbs, close her eyes, and begin to breathe slowly and more slowly, and finally appear to cease breathing altogether, until the attendants would almost believe she had actually died. She would remain in this cataleptic state a short time, and then come to and report what she saw while "dead."

Another article by Hall on the same subject, "The delirium and hallucinations of digitalis," appeared in 1905.

One of the most brilliant contributors to surgery of the vascular system is Rudolph Matas (1860–) (see special biography), of New Orleans. He received the degree of Doctor of Medicine from Tulane Medical School in 1880, was professor of surgery at his alma mater from 1895 to 1927 and since then has held the post of emeritus professor. Dr. Matas has received many honors and honorary degrees from medical institutions and organizations throughout the world and was the first to receive the Distinguished Service Medal of the American Medical Association, conferred in 1938. He is still remarkably active and during the last decade or more has been diligently applying himself to the writing of a comprehensive "History of medicine of Louisiana" which already comprises at least ten unpublished volumes.

In 1888, Dr. Matas published his first account of a new method for the surgical cure of aneurysm. This article, "Traumatic aneurysm of the left brachial artery (illus.). (First application of the intrasaccular suture)," appeared on October 27, 1888. However, the first comprehensive report of this method did not appear until 1902. In this work, Dr. Matas detailed his method of "endo-aneurysmorrhaphy," which was published under the title, "Operation for the radical cure of aneurysm; based upon arteriorraphy (illus.)."

In a recent publication reviewing his own experiences in surgery of the vascular system, Dr. Matas interestingly related the circumstances of the discovery of his method. The following quotation is of historical importance.

> . . . In this case, the successive ligation of the main artery on the proximal and distal poles of the aneurysm had been followed by relapse, and it seemed to me, then, that I had no other alternative but to extirpate the sac. When I exposed the sac and emptied its contents, the failure of the ligations to control the circulation was easily explained by the appearances at the bottom of the sac of three large orifices corresponding to the collateral branches which opened into the sac in the segment of the artery included between the ligatures. It was evident that it was these collateral orifices that fed the sac despite the ligatures that had been placed at each one of its poles. I, at first, intended to secure these collaterals by excising the sac, but the branches of the brachial plexus of nerves were so densely incorporated in its walls that I could not have dissected them out and detached them, without serious damage, thereby paralyzing the arm. It occurred to me then that the easiest way out of this awkward dilemma was *to seal the orifices of all the bleeding collaterals by suturing them as we would an intestinal wound,* leaving the sac attached and undisturbed in the wound. This procedure was at once put into effect and the hemostasis was so perfect and satisfactory that it seemed to me strange that no one should have thought of so simple an expedient before.

In 1900, Dr. Matas published an extensive monograph, "The treatment of abdominal aortic aneurism by wiring and electrolysis. A critical study of the method based upon the latest clinical data."

From 1888 to 1940, Dr. Matas contributed 108 important articles dealing with surgery of the vascular system.

It is of singular significance that the early important contributions heralding the cardiovascular progress of the twentieth century dealt with surgical procedures. This is of particular interest in view of the remarkable progress that has occurred in this field during the last decade. In 1902, Ludolf Brauer (1865–   ), of Marburg and Heidelberg, advocated the resection of ribs together with the costal cartilages in cases of adherent mediastinopericarditis in which adhesions to the thoracic wall occurred. From Brauer's description of the two patients who were the basis for his report, they did not represent instances of chronic constrictive pericarditis. Marked systolic retraction of the left lower anterior portion of the thorax alternating with a corresponding diastolic expansion was present. Collapse of the cervical veins during diastole was observed, the liver was enlarged and circulatory stasis was pronounced.

Brauer reasoned that if a portion of the thoracic cage was resected the heart could contract without pulling the bony structures. He referred to the surgical procedure as "kardiolysis." The operations were performed respectively by Petersen and Simon, of Heidelberg, and both patients showed marked improvement. This report was published in Brauer's article, "Ueber chronische adhäsive Mediastino–Perikarditis und deren Behandlung," in 1902.

A year later, Brauer reported on the progress of the two previously reported patients and the addition of a third patient. One of the aforementioned patients had died a year after operation from influenzal pneumonia and postmortem studies had been conducted. From his clinical experience and from the postmortem findings, Brauer concluded that in the selection of patients suitable for this surgical procedure, the cardinal indication was the presence of systolic retraction over a broad area of the thorax.

Brauer stated that the decortication principle recommended by Delorme was attended by too great a risk although he implied that this

Professor Willem Einthoven and students.

question was one for the future to be determined by the close co-operation of the clinician and the surgeon.

Seven years after Roentgen's discovery of the x-rays and six years after Francis Henry Williams' important article on the application of this method of examination in relation to diseases of the heart and aorta, Friedrich H. L. Moritz (1861–1938) of Germany, introduced the method of orthodiagraphy. By utilizing the roentgenoscope, he traced the shadows cast by the heart and great vessels on a thin sheet of paper. The advantages of this method were the visualization of the beating heart so that the true junctional relationships of the heart and its

large vascular tributaries could be delineated. Orthodiagraphy is a method still frequently employed.

Moritz's article appeared in 1902 under the title, "Ueber orthodiagraphische Untersuchungen am Herzen."

One of the most important innovations of the century was contributed by Willem Einthoven (1860–1927) (see special biography), of Leyden. Professor of physiology at the University of Leyden, he held this post from 1886 to the time of his death. Einthoven's most outstanding work was the adaptation of the string galvanometer for recording the action currents of the heart. His demonstration established the science of electrocardiography. This work appeared in 1903 in his article, "Die

Professor Willem Einthoven in his laboratory.

galvanometrische Registrirung des menschlichen Elektrokardiogramms, zugleich eine Beurtheilung der Anwendung des Capillar-Elektrometers in der Physiologie."

While much of the groundwork relating to electrophysiology had been prepared by the investigations of Galvani (1737–1798), Schweigger (1779–1857), Matteucci (1811–1868), Ernst (1795–1878) and Eduard Weber (1806–1871), von Kölliker (1817–1905), Bowditch (1840–1911), Waller (1856–1922) and MacWilliam (1857–1937), Einthoven's work actually represents the true beginning of the electrocardiograph and of electrocardiography.

He contributed many articles pertaining to electrocardiography. Among them was one of special importance which dealt with the calcu-

lation of the electrical axis of the heart by means of the equilateral triangle (Einthoven's triangle). This work, in collaboration with G. Fahr and A. de Waart, appeared under the title, "Über die Richtung und die manifeste Grösse der Potentialschwankungen im menschlichen Herzen und über den Einfluss der Herzlage auf die Form des Elektrokardiogramms," in 1913.

No modern physician can doubt the importance of Einthoven's contributions, for it is apparent to all that electrocardiography, when utilized wisely and when properly correlated with clinical findings, has been responsible for remarkable progress in the field of cardiology.

Another important contributor of the opening years of the twentieth century was Karel Frederik Wenckebach (1864–1940) (see special biography), of Groningen and Vienna. A graduate of the University of Utrecht, he received the degree of Doctor of Medicine in 1888. A student of Theodor Wilhelm Engelmann (1843–1909), Wenckebach undoubtedly derived much of his interest in the study of the heart from this great teacher.

He established practice in the little Dutch town of Heerlen in 1892 and while there became interested in the arrhythmias of the heart. In 1901, Wenckebach was appointed professor of internal medicine and chief of the clinic at Groningen, in 1911 assumed the same post at the University of Strasbourg, and in 1914 succeeded von Noorden as chief of the first medical clinic at the University of Vienna.

While at Groningen, Wenckebach began his investigations of the arrhythmias and of cardiac conduction in man. In 1903, he produced an important study on premature ventricular contractions of the heart with reference to the resulting compensatory pause. This article appeared under the title, "Ueber die Dauer der compensatorischen Pause nach Reizung der Vorkammer des Säugethierherzens." Five previous publications dealing with cardiac arrhythmias had been published from 1899.

In 1906, utilizing Mackenzie's ink polygraph, Wenckebach demonstrated the first records of dropped beats when the conduction time was fixed. He showed that, when retardation of auriculoventricular conduction occurred, periodic dropping of ventricular beats took place. These pauses in the rhythm of the heart are still known as "Wenckebach periods." These results were published as "Beiträge zur Kenntnis der menschlichen Herztätigkeit."

Wenckebach described a band of muscle fibers in the human heart in the sulcus terminalis of the right auricle which he surmised might represent a path of conduction from the sino-atrial node to the auricle. He also suggested that auricular fibrillation might represent a form of sino-atrial block.

In 1912 Wenckebach noted that quinine at times quieted the violent

Aschoff's most celebrated work dealt with the myocardial changes occurring in rheumatic fever. He described the perivascular cellular bodies which still today are known as "Aschoff nodules" or "Aschoff bodies." The conclusions in the article by Aschoff are as follows.

. . . (1) that the enlargement of the heart muscle in valvular insufficiency produces a true hypertrophy, and (2) that inflammatory changes do not have the described significance and do not explain the decrease in efficiency of the hypertrophied muscle, but that the heart muscle weakens and we are unable to observe by means of our present-day laboratory aids, degenerative changes of a greater extent in the muscular substance. And a circumscribed lesion of the atrioventricular bundles does not enter into the consideration of the cases thus far studied.

This work appeared in his publication, "Zur Myocarditisfrage," 1904.

Sir Arthur Keith.

In 1902, Aschoff published an important study on Ehrlich's side-chain hypothesis with reference to its application in artificial immunization. Aschoff attracted students from many countries and many of them were Japanese. Together with his student, Sunao Tawara, he described the conduction system of the mammalian heart. A later work, in 1937, concerned the conduction system in relation to congenital anomalies of the heart. Aschoff's other contributions dealt with a great variety of subjects in the field of pathology.

By painstaking histologic studies, Sunao Tawara (1873–), one of Aschoff's Japanese students, made monumental contributions pertaining to the conduction system of the heart. He carefully traced out the communications described by the younger His and their junction with the fibers and cells described earlier by Purkinje. During this investigation he discovered the auriculoventricular node (node of Tawara), which added greatly to the existing knowledge of the conduction system of the heart. These results were published in Tawara's monograph, "Das Reizleitungssystem des Säugetierherzens," 1906.

It is an interesting coincidence that in the next year two British scientists, Sir Arthur Keith (1866–), of London and Aberdeen, and Martin William Flack (1882–1931), of London, should also contribute an important study on the origin and conduction of the cardiac impulse.

Sir Arthur Keith was an anatomist and anthropologist of note, a careful investigator and a great teacher. He received many honors

throughout his long career. Flack was pre-eminently a physiologist.

In 1907, a year following Tawara's important publication, Keith and Flack confirmed his findings. They undertook to determine the evolution of the auriculoventricular conduction system and also to search for an area in the right auricle, similar to Tawara's node in the auriculoventricular junctional area, which might represent the area where the heart beat arose. At this time, the opinion was correctly held that the origin of the heart beat occurred in the region of the right auricle near the junction of the superior vena cava and the auricle. In all the mammalian hearts studied, Keith and Flack found a little node of specialized tissue at the anticipated site, which they named the "sino-auricular node" and which has become known as the "node of Keith and Flack."

They presumed the node to be the site of impulse origin but did not prove this to be the case and it was not until 1910 that this proof was provided by the studies of Sir Thomas Lewis.

Keith and Flack's important work appeared as "The form and nature of the muscular connections between the primary divisions of the vertebrate heart," 1907.

Martin Flack.

Among Keith's other works were "An introduction to the study of the anthropoid apes," in 1896; "Ancient types of man," in 1911; "The antiquity of man," in 1915 and 1925; "Nationality and race from an anthropologist's point of view," in 1919; "Concerning man's origin," in 1927 and "New discoveries relating to the antiquity of man," in 1931.

A generous contributor to cardiology and an outstanding personality of all time was "The Beloved Physician," Sir James Mackenzie (1853–1925) (see special biography), of Burnley and London. He graduated from the University of Edinburgh in 1878 and then established practice in Burnley as assistant to Drs. John Brown and William Briggs. Early in his practice, when one of his patients died suddenly and unexpectedly during childbirth, Mackenzie determined to make a thorough study of the heart. He became particularly interested in cardiac arrhythmias and sought a more precise method of studying them. He adapted a Dudgeon sphygmograph to his needs and finally constructed his famous ink polygraph.

After spending thirty years at Burnley, Mackenzie moved to London and gradually developed a large consultation practice. In 1918, he retired from active practice and established The Institute for Clinical Research at St. Andrews, Scotland, where he continued to work until his death.

Mackenzie's outstanding contributions dealt with the cardiac arrhythmias and their separation into types. Especially noteworthy were his studies dealing with auricular fibrillation. He related the case of a woman he had observed in 1880, when she suffered from rheumatic fever. Later he found evidences of cardiac damage. A presystolic murmur was present at that time. As the years passed the mitral obstruction became progressively more marked and the patient's condition worse. Mackenzie was amazed to find that the presystolic murmur had disappeared when cardiac arrhythmia supervened. He was temporarily at a loss to explain this phenomenon. The following quotation from his book demonstrates his clear reasoning in respect to this problem.

> . . . As it was clear that the auricles could not have contracted during the normal period—that is to say, immediately before ventricular systole—the only alternative I could see was that they contracted during ventricular systole. As, in the meantime, I had studied several hundreds of cases and had seen this condition start under a variety of circumstances, particularly in individuals with frequent extrasystoles, I put forward the view that ventricles and auricles contracted together, and assumed that the stimulus for contraction arose in some place that affected auricles and ventricles simultaneously. As at this time I could not conceive of any other possibility to explain the facts, I suggested that the stimulus for contraction arose in the auriculo-ventricular node; and I called the condition "nodal rhythm," under which name the clinical aspects of auricular fibrillation are described in the two editions of this book, the first being published in 1908.

The foregoing is from a third edition of Mackenzie's book, "Diseases of the heart," published in 1914. Other works of Mackenzie were "The study of the pulse," in 1902; "The future of medicine," in 1919; an excellent monograph on "Angina pectoris," in 1923 and his final work, "The basis of vital activity," published in 1926, a year after his death.

Mackenzie accepted the ischemic origin of angina pectoris in its relation to obliterative disease of the coronary arteries. He stated,

> That a muscle should evoke disagreeable symptoms when overfatigued is a principle applicable to all muscular structures of the body. In looking at the coronary arteries in certain typical cases of angina pectoris, one can reasonably infer one way in which the attacks are brought about. In some cases the coronary arteries are so narrowed as scarce to permit the entrance of a pin. During life the stream of blood must have been greatly reduced, and if it were sufficient to supply the muscle during rest, it was demonstrably insufficient while the heart was in a state of activity. In this respect there seems to be a distinct affinity between the origin of the pain in these cases, and in those cases of what is called intermittent claudication.

Mackenzie suffered from angina pectoris for many years and ultimately died from acute infarction of the myocardium. An ancient cardiac infarct was also found at postmortem examination.

A prophetic article was published by John C. Munro (1858–1910), a surgeon of Boston, in 1907. Nineteen years previous to his publication, he had performed a postmortem examination on an infant who had died of heart failure consequent to a patent ductus arteriosus. In the following quotation Munro expressed his interesting predictions.

> . . . After death, which took place without oedema or marked cyanosis, examination showed an open ductus arteriosus lying easily within reach behind the sternum, without any other defect or lesion except a dilated right ventricle. The simplicity of the remedy was so striking that I at once made further dissections, and satisfied myself that it would be possible to ligate the duct provided a diagnosis could be made beforehand. . . .
>
> . . . The operation I would propose, as demonstrated on the cadaver, is as follows: Under ether, which I prefer to chloroform in any case involving collapse of the lung, the sternum can be easily split along its centre or a little to the right, opposite the second costal cartilage. This is easily done with a knife. The sternal halves are then retracted, ample room for working being obtained. The right pleural cavity will probably be opened but the left one will not. Judging from analogous cases in surgery, this should not be serious, but if necessary the physiologist's apparatus for maintaining artificial respiration could be employed. I hardly believe that it would be needed. After retracting the thymus upward, the pericardium is exposed. Its reflection lies so high on the large vessels that the ductus to all intents and purposes is intra-pericardial. In the upper angle the aorta will be seen on the patient's right and the pulmonary artery on the left. By following close to the aorta toward the under surface of the arch the ductus, as large as the aorta itself, will be seen as the first vessel to the left pointing upward and a little to the right. Both pulmonary branches lie too far posteriorly to be seen, and by keeping close to the aorta the main pulmonary trunk will escape injury. On pushing through the tissues by blunt dissection the ductus, theoretically, should be easily surrounded with a ligature. It is a question whether or not simply crushing it would not accomplish as much, and in case of necessity, I believe that it would be worth trying. After closing the anterior pericardial wound the sternum can be sutured or not and the skin closed. . . .

William Sydney Thayer.

It is of interest to note that the first successful ligation of a patent ductus arteriosus did not occur until thirty-two years later when Gross and Hubbard reported their case (1939).

Another contributor to knowledge related to the heart and its diseases was the prominent teacher and clinician, William Sydney Thayer (1864–1932), of Milton, Massachusetts. He became professor of clinical medicine at Johns Hopkins University and held this post for many years.

One of Thayer's interesting observations dealt with the third heart sound, which he discussed at a meeting of the Medical Society of the County of Kings on March 17, 1908.

He stated that in certain young persons whose chest wall was not thick, palpation detected a slight shock independent of, and following, the cardiac impulse. By means of auscultation, a third heart sound was audible, occurring shortly after the second heart sound during the phase of diastole. This third heart sound had the character of a dull and distant thud. Thayer had observed this phenomenon in twenty-four cases. To all intents and purposes the patients were perfectly healthy individuals. He had also detected a third heart sound in a dog and at post-mortem examination the dog's heart was found to be normal.


Leo Buerger.

By means of cardiograms and plethysmograms, Thayer found that the third heart sound was coincident with the slight rise occurring in the early part of the diastolic curve and with the shoulder of the jugular venous curve. While not certain as to the exact mechanism responsible for the production of the third heart sound, Thayer suggested the following hypothesis: At the end of the ventricular contraction, with the first rush of blood into the ventricles from the auricles, during diastole, the impact of the blood against the upper surface of the flaps of the auriculo-ventricular valves sets them in vibration. It is this vibration that produces the third heart sound. The title of this address was "The early diastolic heart sound."

In 1905 Thayer had demonstrated endocarditis as a sequela to gonorrheal septicemia. This article appeared as "On gonorrhoeal septicaemia and endocarditis." Again, in 1922, he wrote on the same subject and called attention to the fact that at times gonorrheal endocarditis followed a subacute course. Toward the close of the nineteenth century, Thayer extensively investigated malaria, demonstrated eosinophilia in trichinosis and wrote extensively on many phases of medicine.

In 1908 Leo Buerger (1879–1943), of New York, a pupil of Libman, published his classic account of thrombo-angiitis obliterans, frequently referred to as Buerger's disease. While von Winiwarter had noted the disease in 1879, Buerger's report was the first complete dissertation on

the subject considering the symptoms and the pathology of the disease. This work appeared in 1908 under the title, "Thrombo-angiitis obliterans: a study of the vascular lesions leading to presenile spontaneous gangrene." Buerger called attention to the frequent although not exclusive occurrence of the disease among Polish and Russian Jews. The following quotation from his article is appropriate.

> Viewing the process from the standpoint of the pathological lesions, and considering certain facts obtained by clinical observation, it would seem most plausible to assume that certain territories of either the arteries or the veins become rather suddenly thrombosed, in a fashion similar to the thrombotic process that occurs in the superficial veins of the lower extremities. Thus, at one time the dorsalis hallucis and dorsalis pedis, or perhaps plantar arteries or veins, could become closed by a red clot; and then the process of organization would take place. Perhaps after an interval of weeks or months a similar process would cause extension upward, or affect other arteries and veins, until, after a lapse of many months, or a year or more, practically all the larger vessels would become occluded. It is from a study of the age of the process in the various territories that we are led to this supposition. Here too as in the superficial thromboses there is more tendency for the larger vessels to be involved than for the very fine ones; and although the process seems to ascend, it probably does not originate in the capillaries or small arterioles, but begins in branches of moderate size. The attendant periarteritis could be regarded as being either secondary or, possibly, as being produced by the same causes that lead to the thrombosis. Certain it is that the periarteritis is intimately linked with the presence of occluding masses.

Maude E. Abbott.

The most extensive contributor to knowledge relating to congenital anomalies of the heart was Maude E. Abbott (1869–1940), of Montreal. In 1899, she was appointed curator of the McGill Museum and at that time became intensely interested in congenital anomalies of the heart. An unlabeled specimen in the laboratory (a three-chambered adult heart), regarding which few or no data were available, interested Dr. Abbott. Her curiosity led to correspondence with Osler, then at Johns Hopkins University, who replied that he remembered the specimen and had frequently used it in his teaching while at McGill and that the case had been reported in 1824 by Dr. Andrew Holmes.

Maude Abbott's interest in congenital cardiac anomalies soon became well known and she received specimens from far and wide for exact identification. This gave her the greatest opportunity yet afforded any

physician to amass not only a remarkable collection of abnormal hearts but to utilize such material wisely and to acquire a specialized knowledge never before attained. There can be no doubt that Maude Abbott's teaching and influence were directly responsible for converting the mysticisms and uncertainties of what was believed about congenital cardiac anomalies into understandable realities. Through her work the clinical diagnosis of these defects has become remarkably precise and has enabled the present-day surgeon to intervene, so that an ever-increasing number of hitherto incurable patients are now finding relief.

In 1908, Abbott published her classic monograph reporting 412 cases of congenital cardiac disease gathered from her own material and from the medical literature. This important work, "Congenital cardiac disease," appeared in Volume IV of Osler's "Modern Medicine." Numerous individual articles appeared, and in 1936 her remarkable "Atlas of congenital cardiac disease" was published under the sponsorship of the American Heart Association. It contains a critical analysis of 1,000 cases of congenital cardiac anomalies.


W. A. Jolly.

The first clinical recognition of auricular flutter was recorded by A. F. Hertz and G. W. Goodhart (1845–1916), of England, in 1909. MacWilliam had observed the phenomenon in his experiments on the faradization of the animal heart in 1887. Hertz and Goodhart studied patients who had the disorder and noted that the remarkably rapid auricular movements were visible by means of the roentgenoscope and audible by means of the stethoscope although their extreme rapidity (300 beats each minute or more) defied counting them. In cases in which the ventricular rate was not excessively rapid (in which functional auriculoventricular block occurred) the auricular waves were depicted in jugular curves. Hertz and Goodhart's work appeared in the article, "The speed-limit of the human heart."

Two years later further observations on auricular flutter were recorded by W. A. Jolly (1877–1939) and W. T. Ritchie (1873–   ), of England. Later Jolly became professor of physiology at the University of Capetown, a post which he held for twenty-seven years. These workers

named the condition "auricular flutter." Jolly and Ritchie were of the opinion that the discrepancy in ventricular and auricular rate in one of their cases was the result of organic disease of the auriculoventricular bundle. Their article appeared under the title, "Auricular flutter and fibrillation." In a later publication, Ritchie expressed the opinion, following microscopic study of the heart in a case in which auricular flutter had been present, that a lymphocytic infiltration of the pericardium in the region of the sinus node, which he observed, may have depressed its function and accounted for the abnormal acceleration. These comments were expressed in his article, "Further observations on auricular flutter," 1913.

Shortly after Mackenzie and Hering published their accounts on the arrhythmia ultimately to become known as "auricular fibrillation," Carl Julius Rothberger (1873–) and Heinrich Winterberg (1871–), of Germany, presented an interesting discussion of the condition. Their work preceded Sir Thomas Lewis' account by only a few months. Like Lewis, Rothberger and Winterberg showed that this arrhythmia occurred in human beings. They also referred to the disorder as "pulsus irregularis perpetuus."

By means of venous pulse tracings, Rothberger and Winterberg demonstrated that the waves of auricular activity were absent and that the phlebogram showed the positive or ventricular form of venous pulse. Their records were identical with the experimentally produced curves of auricular fibrillation (Vorhofflimmern). Descriptions of their electrocardiograms were characterized by total arrhythmia of the ventricles, absent P waves and the presence of irregular undulations due to the fibrillary activity of the auricles. Their work appeared in 1909 under the title, "Vorhofflimmern und Arhythmia perpetua."

One of the greatest clinicians and teachers of all time and a significant contributor to the field of cardiology was Sir William Osler (1849–1919) (see special biography). Born in the small Ontario community of Bond Head, he lived variously in Canada, the United States and England. A graduate of McGill University in 1872, Osler studied under such celebrated teachers as R. Palmer Howard, Adam H. Wright, Duncan MacCallum and J. Morley Drake. The next two years were spent in graduate study in England, Germany and Austria.

In 1874 Osler was appointed lecturer on medicine at McGill University. Two years later he became pathologist to Montreal General Hospital and in 1878 became full-time physician to this hospital. After two visits to England, Osler was appointed professor of clinical medicine at the University of Pennsylvania in 1884. Five years later he accepted the same position at the newly founded medical school at Johns Hopkins University and held this chair until his appointment as Regius Professor of Medicine at Oxford University in 1904. While he

was at Hopkins, medical education made rapid and notable progress, to which Osler and his famous contemporaries, William Welch, W. S. Halsted, Henry M. Hurd and Howard A. Kelly, all gave noteworthy impetus.

Almost countless honors were bestowed on Osler during his brilliant and productive career and in 1911, at the coronation of George V, he was created a baronet.

One of Osler's outstanding contributions was his account of "Chronic infectious endocarditis," which appeared in 1909. In addition to giving a splendid description of the disease now known as "subacute bacterial endocarditis," he described the evanescent painful embolic subcutaneous nodules (pathognomonic of the disease) since known as "Osler's nodes." These nodes had been noted before but their significance and specific occurrence in cases of subacute bacterial endocarditis had not been established.

Edward Carl Rosenow.

In 1892, Osler's great work, "The principles and practice of medicine," was first published. It went through many editions and is still a standard textbook. Fifteen years later (1907) the first three volumes of Osler's famous "System of modern medicine" were printed.

Osler's comments on the hereditary factor of angina pectoris appeared in 1896. The following quotation is of interest.

> True angina is an arterial incident, and, as we know that the members of certain families show a special tendency to arterial degeneration, it is not surprising to find cases in father and son, or in brothers, or even in representatives of three generations. There are some remarkable instances on record in which many members of a family have been attacked. The first, and one of the most notable, is that reported by Dr. Robert Hamilton, in which the father of a patient, a young man aged twenty-four, two brothers and one sister were affected. In all, the disease developed in early life; in Hamilton's own patient, at the twelfth year. It is quite possible from his description that the disease may not have been angina pectoris, but spasmodic asthma associated with pain. [See Hamilton reference under 1785 in main text.]

Pioneer studies dealing with the bacteriology of endocarditis were conducted by Edward Carl Rosenow (1875–), of Chicago and Rochester, Minnesota. He became head of the Division of Experimental Bacteriology and professor of experimental bacteriology at the Mayo

Foundation for Medical Education and Research in 1915 and held these positions until his retirement in 1944.

In 1909 Rosenow conducted experiments on the production of endocarditis in animals using both pneumococci and staphylococci. The micro-organisms which he believed were pneumococci were ultimately shown to be streptococci. His first article on this subject was titled, "Immunological and experimental studies on pneumococcus and staphylococcus endocarditis ('*chronic septic endocarditis*')." Three years later his article "On the mechanism of production of infectious endocarditis" appeared. These and similar studies were continued and amplified and Rosenow stressed the role of streptococci in endocarditis. He was the originator of the hypothesis of elective localization of streptococci and the hypothesis of mutation of streptococci.

Without a doubt the most outstanding contributor to both experimental and clinical electrocardiography was Sir Thomas Lewis (1881–1945), of London (see special biography). He was a great teacher, a critically precise investigator and a sound clinician, a combination of scientific qualities not commonly possessed by one man. Lewis was a graduate of the University College of Cardiff and the University College Hospital Medical School of London. A prolific investigator and writer, Lewis attracted students from all over the world, many of whom today continue to perpetuate his principles and teachings. He received many well-merited honors and was knighted in 1921.

One of Lewis' outstanding contributions dealt with auricular fibrillation (at that time an imperfectly understood condition). He showed that this disorder occurred frequently in man and he brought forth certain fundamental facts regarding its nature. This classic article, "Auricular fibrillation: a common clinical condition," appeared in 1909, the same year that Rothberger and Winterberg's work appeared. In this article, Lewis conclusively demonstrated that auricular fibrillation and nodal rhythm were two dissimilar conditions. (Mackenzie had previously suggested that this total arrhythmia might be due to nodal rhythm.) Lewis showed that the totally irregular pulse commonly observed in cases of mitral stenosis was due to fibrillation of the auricles.

Lewis called attention to the completely disorderly rhythm and demonstrated that the amplitude of the beats does not correspond to the pauses which precede them and that the experimental production of fibrillation of the auricle results in similar response of the ventricles. He described the electrocardiographic characteristics of auricular fibrillation and showed that the waves in experimental tracings corresponded to the fibrillary movements in the auricle.

In 1920 and 1921, Lewis and his students published a series of eleven important articles demonstrating the mechanism of circus movement in cases of auricular fibrillation and flutter and the differences between them (see references).

Earlier, in 1910, he had verified Keith and Flack's hypothesis that the sino-auricular node is the seat of origin of the cardiac impulse. This proof was established by electrocardiographic investigation and appeared in the article, "The pacemaker of the mammalian heart as ascertained by electrocardiographic curves."

In 1911 appeared Lewis' first book, "Mechanism of the heart beat," and in 1921, a much amplified volume, "The mechanism and graphic registration of the heart beat." He contributed approximately sixty-three articles dealing with electrocardiography and in his later work wrote extensively on the clinical aspects of heart disease, peripheral vascular diseases and the treatment of cardiac disorders.

Emanuel Libman.

Lewis was editor of "Heart" from 1909 to 1927 and was one of its most prolific contributors. Like many cardiologists, Lewis died of coronary disease; his death occurred following the fourth myocardial infarct in eighteen years.

A brilliant American clinician, whose studies did much to clarify the problem of the endocarditides, was Emanuel Libman (1872–1946), of New York. An impressive teacher and a great clinician, his colorful personality and almost instant decision clearly set him apart from his contemporaries. Always ready to discuss any subject in medicine, Libman's readiness in this respect and his scholarly comments livened many medical meetings. He was professor of clinical medicine at Columbia University for many years and during his active years developed a large consultation practice.

In 1910 Libman, in collaboration with H. L. Celler, published his important article on what he then called "subacute infective endocarditis." He emphasized the insidious onset of the disease and its protracted course and stressed particularly its embolic manifestations. He discussed the cultural characteristics of the recovered streptococci in detail and compared them with other micro-organisms. Libman further discussed the difficulties encountered in classifying the streptococci. The following quotation is of interest:

We have shown the difficulties that are encountered in an attempt properly to classify the organism which we have met in our cases. We have also shown that organisms which are practically the same as the group which does not ferment

inulin have been found by us in local infections of various kinds. The important point to be brought out is that up to the present time whenever we have found the organisms which we have usually called endocarditis cocci par excellence (or attenuated streptococci of endocarditis) there was always present an infection of the endocardium. In no other disease have we found these organisms in the blood current. They, therefore, seem to have diagnostic importance.

This work appeared in the article, "The etiology of subacute infective endocarditis," in 1910.

In an earlier publication (1906) Libman had reported on a case of (subacute bacterial) endocarditis with multiple mycotic aneurysms.

In 1913 Libman published an interesting and important report, in which he described the bacteria-free stage of subacute bacterial endocarditis. He described cases in which patients had passed through the bacterial stage of the disease and the infection had subsided spontaneously but in which the havoc of the infection had resulted in subacute or chronic glomerulonephritis, splenomegaly, emboli and progressive anemia. These patients had recovered from the valvular infection but continued to fail and ultimately died from the damage wrought to other vital parts of the body.

In 1924, in collaboration with Benjamin Sacks, Libman produced his important article on "A hitherto undescribed form of valvular and mural endocarditis." Four cases composed the basis of the study. The lesions found involved all four valves and the mural endocardium and did not resemble those of subacute bacterial endocarditis, rheumatic endocarditis or any other form of endocarditis. The name "atypical verrucous endocarditis" was applied to the disease. Blood cultures did not reveal the presence of micro-organisms and the vegetations were free of bacteria. Pericarditis was present. The disease attacked young persons and in two of the four cases eruptions on the face resembling acute disseminated lupus erythematosus were present. The etiologic agent was unknown but the suggestion was made that future studies should include the investigation of filtrable viruses and spirochetes. This form of endocarditis has become known as "Libman-Sacks disease."

Libman also wrote extensively on coronary thrombosis.

While the problem of bacterial endocarditis was gradually becoming more clear, many unsolved questions remained. Among them was the question why the same micro-organism should in certain patients produce acute endocarditis while in others the endocarditis was subacute or chronic. In 1910 Hugo Schottmüller (1867–1929), of Germany, reported his experience with the so-called chronic cases, which he referred to as "endocarditis lenta," and contributed data which helped to clarify this perplexing problem. He had uniformly isolated a micro-organism which he believed merited a separate classification owing to its remarkably characteristic cultural behavior. Schottmüller called it "Streptococcus viridans." This micro-organism coincided with the "Streptococcus parvus" described and named by Lenhartz, the "Streptococcus

endocarditidis" isolated by Libman and the "modified pneumococcus" described by Rosenow. From this time on the characteristics of this disease and its relationship to this peculiar streptococcus became progressively well known.

Important studies dealing with the muscular architecture of the ventricles were contributed by Franklin Paine Mall (1862–1917), of Belle Plaine, Iowa, and Baltimore. One of the outstanding anatomists and embryologists of America, a pupil of Wilhelm His, Sr., and Carl Ludwig, Mall became professor of anatomy at Johns Hopkins University.

Mall applied his extensive knowledge of embryology in his investigation of the arrangement of the muscle fibers of the ventricles with special reference to the systolic function of these chambers. He stressed the point that the heart in its development from the primary cardiac tube is invested with a longitudinal as well as a circular muscular layer in the same manner as other vascular structures are endowed. As fetal development progresses, the cardiac tube becomes twisted to assume the form of a letter **U**. Still further in the progress of development, when the interventricular septum comes into being, the **U** arrangement simulates that of a **W**, the arms of which become rotated, much in the manner of a twisted rope. The complex arrangement of the musculature, Mall ascribed to a functional adaptation.

Franklin Paine Mall.

Mall and his students demonstrated that the musculature of the ventricles of mammals and man could by careful dissection be unrolled like a scroll. Mall showed that the musculature of the two ventricles is made up of two distinct spirals, the one coursing from the tricuspid or sinus portion of the heart to the apex of the right ventricle (sinospiral) and the other from the aortic and mitral area to the apex of the left ventricle (bulbospiral). These two systems of spiral muscles are each composed of a deep and a superficial layer. They run at right angles to each other and intercommunicate by twisted strands which course from the papillary muscles of one ventricle to the other. This important work appeared in 1911 in Mall's article, "On the muscular architecture of the ventricles of the human heart."

Mall is also known for his work in the pathology of early human embryos and his studies on monsters and the structural unit of the liver.

The first truly representative and influential account regarding the clinical recognition of coronary thrombosis was that of James Bryan Herrick (1861–), of Chicago. A graduate of Rush Medical College in 1888, he became professor of medicine at his alma mater and held this position from 1900 to 1926. Herrick has received many well-merited honors and in 1939 was the second outstanding American to receive the Distinguished Service Medal conferred by the American Medical Association.

In 1912 appeared Herrick's classic account of coronary thrombosis, "Clinical features of sudden obstruction of the coronary arteries." While the reports of Hammer and Dock preceded Herrick's publication, neither of the previous publications was as comprehensive nor did they attract the same degree of recognition. Herrick's article coincided with a clearer understanding by the medical profession of America of the clinical recognition of this hitherto unrecognized disease. Instances of correct diagnoses became more frequent but nearly a decade passed before the recognition of coronary thrombosis became almost a routine procedure.

James Bryan Herrick.

In addition to calling attention to the clinical features of coronary thrombosis, Herrick emphasized the important point that the disease is not always fatal. He showed that angina pectoris frequently exists some time prior to the sudden obstruction of a coronary artery, although instances occur in which the first evidence of disease is the obstructive episode.

In 1919 Herrick reported a case of coronary thrombosis which was studied by means of electrocardiographic records. Here he called attention to the diagnostic significance of T wave inversions and the alterations of their contour. The diagnosis was corroborated by postmortem examination. This article appeared under the title of "Thrombosis of the coronary arteries."

Herrick wrote extensively in the field of medicine and contributed most generously to knowledge of diseases of the heart. In 1942 he published "A short history of cardiology."

An important study dealing with the early pathologic manifestations of arteriosclerosis was contributed by Oskar Klotz (1878–1936), of Preston, Ontario, and later of Montreal, Pittsburgh and Toronto. A graduate of McGill University in 1906, he also took graduate training at the University of Bonn. Klotz was professor of pathology and bacteriology at the University of Pittsburgh from 1910 to 1920 and professor of pathology, under auspices of the Rockefeller Foundation, at São Paulo, Brazil, from 1920 to 1923, when he became professor of pathology and bacteriology at the University of Toronto. Klotz made many important contributions in his field.

In 1912, while at the University of Pittsburgh, in collaboration with M. F. Manning, Klotz published his important article, "Fatty streaks in the intima of arteries." Believing that development of arteriosclerosis could be accurately observed only near the time of its inception, he stressed the importance of examining the arteries of children and young persons. Klotz examined various arteries but he found that the most revealing vessels were the aorta and the arteries arising from its arch. The following quotations are of interest and importance.


Oskar Klotz.

> With a view of determining the earliest stages of the arterio-sclerotic process our attention was attracted to those minute yellow streaks and dots which are so frequently observed in the arteries of young individuals. It is quite useless to argue the questions concerning the development of intimal scleroses if we study and discuss the late changes of the disease alone. . . .
>
> . . . It is evident from these observations that there is direct relation between acute diseases and progressive lesions in the intima of the larger arteries. These lesions, though apparently of little account at the beginning, may become autochthonous and develop definite nodular endarteritis with atheroma. Thus even when the initial factors leading to the fatty streaks are removed a vicious process is established which may lead to a nodular arteriosclerosis or atheromatous ulceration.
>
> We have found no evidence that before the development of the fatty streaks of the aorta a degenerative or other condition in the media is associated with the growth of connective tissue in the intima; but there is every indication that the production of tissue in the intima is the result of a direct irritation of that tissue by the presence of infection or toxins or of the stimulation by the products of a primary degeneration in that layer.

In another important paper, published in 1918, "Some points respecting the localization of syphilis upon the aorta," Klotz emphasized the

importance of the lymphatic structures of the abdomen and thorax in transporting spirochetes to the aorta. He further showed that the regional involvement of the aorta corresponds to the existing abundance of lymphatic vessels in and about the aorta.

In 1914, at a time when considerable confusion still prevailed with respect to the classification of diseases of the heart and, as previously pointed out, vague diagnostic terms were used to designate questionable diagnoses, the important article by Richard Clarke Cabot (1868–1939) appeared. At the time of this publication, Cabot was assistant professor of clinical medicine at Harvard Medical School. The following quotations from Cabot's article are significant.

Richard Clarke Cabot.

> To classify cases of disease according to their pathogenic agent or process, and not solely by naming the region affected or the function disturbed, is the ideal of scientific progress in medicine.
>
> But until the last decade we have made little advance in this direction as regards the diseases which gravely disturb the heart function. Thus we still find in standard textbooks a section devoted to "mitral regurgitation," its diagnosis, prognosis and treatment, although mitral regurgitation is almost as vague a phrase as "spinal paralysis" or "brain fever." Just as a "spinal paralysis" may be due to trauma, to the tubercle bacillus, to the *Spirochaeta pallida*, to the organism of poliomyelitis or to cancer, so "mitral regurgitation" is only a symptom caused by the action of streptococci, by the degenerative lesions of arteriosclerosis, by the muscle-tiring resistance of nephritic hypertension and probably by other causes. . . .
>
> A similar criticism applies to all diagnoses of "myocarditis." The micro-organisms of rheumatism and of syphilis, the ravages of arterial disease and perhaps many other causes may produce the lesions of chronic fibrous myocarditis, with or without recognizable symptoms. A diagnosis of myocarditis is like a diagnosis of "ulcer"; it calls for an etiologic qualification, such as syphilitic or tuberculous.

Cabot's frank discussion of these prevailing inaccurate teachings did much to correct the unfortunate situation. The older clinicians did not change their ways but physicians of the younger generation were impressed and soon a more precise and uniform classification of diseases of the heart came into being. Cabot's article appeared as "The four common types of heart-disease; an analysis of six hundred cases," in 1914.

Cabot taught practical bedside medicine and in 1911 his helpful volume, "Differential diagnosis; presented through an analysis of 385

cases," appeared. This was an extremely useful book for both the student and the practitioner of medicine.

Fundamental principles regarding the physiology of the heart and circulation were established by Ernest Henry Starling (1866–1927), the great English physiologist of London.

In collaboration with S. W. Patterson, of London, and H. Piper, of Berlin, Starling established his famous "law of the heart," that is, the mechanism involved in the adjustment of the heart to the demands of increased work. This important contribution appeared as "The regulation of the heart beat," in 1914. A few quotations from this famous work permit the experimenters to relate their own story:


Ernest Henry Starling.

. . . In our preparation the heart is free from all nervous control. The question arises whether we can refer to one or a few elementary qualities of the muscular tissue the whole behavior of the heart, under stress or light work, when efficient or failing, when stimulated or depressed by drug or nerve. The solution of this question can only be arrived at by accurate analysis of the mechanical phenomena of the heart beat under rigorous control of all conditions. The results of such an analysis, which has occupied us for the last two years, are presented in the following pages. . . .

Every increase in either of these factors [arterial resistance, inflow, rate and temperature] gives an increased diastolic volume of the heart and increased mechanical response at contraction. With a moderate increase in inflow or arterial resistance, the diastolic pressure in the ventricles may be unaltered. If the increase in size during diastole becomes excessive, such an increase can only be produced by an active stretching of the ventricular wall, and we then find that the diastolic pressure, and therefore the initial tension on the muscle fibers at the commencement of contraction, is increased at the same time as the cardiac volume. In every case therefore the reaction of the heart muscle seems to be determind by the length of its constituent fibers at the moment of activity. Changes in initial tension are merely incidental to changes in length.

A great clinician and teacher whose influence profoundly affected medical concepts in the closing years of the nineteenth century as well as in the early years of the present century, was Sir Thomas Clifford Allbutt (1836–1925), Regius Professor of Physic at Cambridge University. Allbutt's contributions dealing with the cardiovascular system were protean and dealt with hypertension (hyperpiesia), arteriosclerosis, angina pectoris and syphilis of the aorta. His years of observation and clinical experience formed the basis for his widely used two volume

set, "Diseases of the arteries including angina pectoris," which appeared in 1915. Allbutt was a gifted writer and few medical authors have ever equalled his eloquent diction. It is therefore fitting that certain pertinent passages from the aforementioned volumes be quoted. Allbutt opposed Huchard's views on the so-called cardiosclerosis (see reference page 197) and summarized his own beliefs pertaining to the effects of what he called hyperpiesia (hypertension) on the heart.

In Hyperpiesia, as we may see again and again, the heart is for a long time little the worse; it has more work to do, but for a while it meets this demand without even a static dilatation or great hypertrophy. For many weeks at least, in comparatively young persons, perhaps for some months or a year, I cannot tell, the heart may meet a pressure of 180–200 without demonstrable overgrowth. A normal left ventricle can continue to expel its contents against a double aortic pressure, as may be shown by the constancy of the diastolic pressure and of the pulmonary arterial pressure. In trained men the heart learns to meet large, though temporary, fluctuations of output.

Sir Thomas Clifford Allbutt.

Allbutt's views concerning the causes of arteriosclerosis were summarized as follows:

Arteriosclerosis in Chronic Bright's Disease

Class A

A (I) Primary intimate intrarenal arteriosclerosis not due to high pressures: in Granular kidney constant; in other kinds inconstant. Found likewise in some other organs.

A (II) Secondary, systemic, arteriosclerosis; consequent on high pressures: as seen also in secondary contracted kidney ("small white"). More visible in main branches.

A (III) A few mixed cases, not originally Bright's disease; such as renal disease supervening on a general arteriosclerosis, whether "Hyperpietic" or "Decrescent." (It is suggested by some pathologists that the primary contracted, or "Granular" kidney, properly so called, may be due not to any toxin but to long prevalence of high arterial pressures.) I am not of this opinion, unless in a very modified form.

Not Bright's Disease

Class B

B (I) The "arteriosclerotic kidney"; an alteration implied in general arteriosclerosis, usually of the decrescent kind without high pressures. An atrophic condition.

B (II) Less frequently, entailed by the consecutive arteriosclerosis of excessive blood pressures (as A (II)).

High pressures may be considered as (I) obligate with primary Granular kidney; (II) commonly associated with other kinds of Bright's disease; (III) independent of Bright's disease (*e.g.* "Hyperpiesia").

B (III) The merely starved kidney of old persons in which fibrosis may be more evident than arteriosclerosis.

The term Bright's disease is used to cover the two or more primary diseases of the kidney.

Allbutt's views regarding angina pectoris were in direct opposition to those of many contemporaries, especially the views of Sir James Mackenzie. Even in this relatively advanced period of the twentieth century much confusion prevailed concerning the true nature of angina pectoris. Allbutt's statements regarding angina pectoris were as follows:

> In this secret and fell disease there is a fascination to which no physician is a stranger, a fascination in its dramatic events and in the riddle to be read. By angina pectoris the humble out-patient is for the nonce lifted up into the sphere of a Hunter or an Arnold; over him we endeavor to bring the old discordant and mutually destructive arguments into some consistency, ringing again the old changes on the old bells. . . .
>
> . . . This much we can say, with some certainty, and on other evidence contained in more than one part of this chapter, that, whatever the mechanism at the neck of the heart and aorta, here is a knot of exalted sensibility to tension. It is my position that angina pectoris consists in a morbid exaltation of this sensibility to tension, felt in the majority of cases at this spot, or more or less onwards in the vessel, rather than in the heart itself; and that according to homology the mechanism for this irritation should be seated not so much in the inner coat of the aorta as in its quasi-cutaneous investment. By this mechanism every wave of tension should be propagated and distributed according to its indications, so that pressure in excess and in defect may be equalized or compensated. It would appear that, however large, these fluctuations—and in vigorous bodily exercises we know that they may be very large—are normally thus redistributed without troubling the sensorium; the balance is automatic. It is when by disease the receptive surface is made abnormally sensitive that these stimuli force their way, as pain, to the sensorium. Happily, the sensorium does not usually become well aware of excessive tensions, say of Bright's disease or of aortic regurgitation, so long as the investment of the vessel remains normal; but if the investment of the ascending aorta—and perhaps of more extensive areas of the compound cardiac-arterial vessel—be by some morbid cause thrown into a hypersensitive state, then we receive, as it were, heated reports of blood pressures, and tension darts into pain, pain which in the coverings of other viscera, in pleura, meninges, peritoneum and so forth, we know only too well may be grievous, but which, when arising in the citadel of life, is terrific.

Allbutt made numerous important contributions dealing with the history of medicine.

The first to demonstrate changes in the T waves of the electrocardiogram of man produced by administration of digitalis was Alfred Einstein Cohn (1879–   ), of New York. Since 1911 he has been associated with the Rockefeller Foundation. In 1914, at the meeting of the College of Physicians of Philadelphia, Cohn presented his work, "Clinical and electrocardiographic studies on the action of digitalis."

In addition to calling attention to the prolongation of auriculoventricular conduction produced by the administration of digitalis, Cohn apparently for the first time described the effect of the drug on the T waves of the electrocardiogram. The following quotation is from his article.

Another new sign in the electrocardiogram is an alteration in the size, shape and direction in the T-wave. The first change noted after the administration of digitalis is usually a diminution of the height of this wave, usually in the third lead first, and later in the second. The change may be noticed as early as twenty-four hours, and at the end of forty-eight hours the wave may become iso-electric, or it may become diphasic. In some electrocardiograms, the T-wave for pathologic reasons is pointed downward. If digitalis is given, the direction of the T-wave during the action of the drug is pointed upward. While the causative factors in the change of the T-wave cannot be precisely explained, the inference is that there is an alteration in the contractile substance of the heart.

Fundamental studies concerned with the cardiovascular response to hyperthyroidism (exophthalmic goiter and hyperfunctioning adenomatous goiter) were contributed by Henry Stanley Plummer (1874–1936), of Rochester, Minnesota. He was a brilliant clinician, a profound thinker and a mechanical genius. Plummer received his medical degree from Northwestern University in 1898 and became a member of the permanent staff of the Mayo Clinic in 1901. He was chief of a section on clinical medicine at the Mayo Clinic and professor of medicine in the Mayo Foundation for Medical Education and Research.

Henry Stanley Plummer.

In 1915 Plummer reported his extensive studies, "Studies in blood pressure. I. Blood-pressure and thyrotoxicosis." At this time he designated exophthalmic goiter as "hyperplastic toxic goiter" and hyperfunctioning adenomatous goiter as "nonhyperplastic toxic goiter." Plummer's analysis of the alterations of blood pressure together with pulse studies and his astute recognition of the other clinical phenomena of hyperthyroidism permitted him and his students to differentiate the forms of thyrotoxicosis accurately in a remarkably high percentage of cases even before advent of basal metabolic determinations. The following quotations from Plummer's article are significant.

. . . The high pulse pressure, with the well-known vasomotor phenomena in exophthalmic goiter, leads to the almost unquestionable conclusion that there is no vascular hypertension in this condition. The high systolic pressure is essential to the maintenance of a normal diastolic blood-pressure in these cases having a low peripheral resistance. In many cases even a normal diastolic pressure is not maintained. That the long-continued intoxication associated with the hyperplastic thyroid may lead to hypertension is probable. Evidence to show this will not be considered in this paper. On the other hand, an unduly open peripheral vascular system is

occasionally present in patients recovered from exophthalmic goiter. The height of the systolic blood-pressure in exophthalmic goiter is somewhat indicative of the degree of intoxication. . . .

. . . That 27 per cent of patients having nonhyperplastic goiter above forty years of age are accompanied by a systolic blood-pressure above 160 eliminates the question of an accidental association. This question has been checked by much data, the publication of which is unnecessary. . . .

Plummer was a pioneer in America with respect to esophagoscopy and bronchoscopy and made many important contributions in this field, in addition to training a group of outstanding students who have since become leaders in this work. Plummer has been particularly known for his investigations dealing with the thyroid but one of his outstanding contributions, inculcated in his many students, was an appreciation of the coexistence of organic disease and associated psychoneurotic manifestations.

The first clinical record of ventricular fibrillation with temporary recovery of the patient was reported by George Canby Robinson (1878–), of Baltimore. In 1917, while dean of the medical school of Washington University in St. Louis, he reported this interesting and unusual case, in collaboration with J. F. Bredeck, under the title, "Ventricular fibrillation in man with cardiac recovery." The patient, a woman forty-five years of age, with symptoms and signs of marked cardiac insufficiency, suffered from three attacks of convulsive syncope. During one of these attacks the electrocardiogram displayed ventricular fibrillation. The patient lived thirty hours after the paroxysm of this disorder had been noted.

Ventricular fibrillation during the process of death had been observed by Halsey, Robinson and Willius.

The first comprehensive account of the cardiac changes at times occurring in myxedema was that of Hermann Zondek (1887–), of Berlin, Privat-Dozent in His's clinic at the Charité. In 1918, under the title of "Das Myxödemherz," he described four cases of high grade myxedema in which the patients were men between the ages of forty-five and fifty-five years. These patients, in addition to presenting the characteristic clinical phenomena of myxedema, also displayed marked evidences of cardiac involvement. These changes consisted in marked enlargement of the cardiac silhouette as revealed by the roentgenogram, slowing of the pulse and alterations in the electrocardiogram. No notable changes in the blood pressure occurred. Zondek's conclusions were as follows (in translation).

The myxedema heart is characterized:

Before treatment with thyroid substance:

1. By a dilatation of the left as well as the right chambers of the heart, which may be extreme.
2. By sluggish heart action, slowing of the pulse and by normal blood pressure.
3. By disappearance of the P and the T waves of the electrocardiogram.

After treatment with thyroid substance:

1. By the disappearance of the marked enlargement of the heart approaching somewhat the normal.

2. By a more active heart action, by significant acceleration of the pulse rate without elevation of blood pressure.

3. By a return of the P and the T waves of the electrocardiogram, and when negative, their return to a positive direction.

In 1913, W. Falta, of Vienna, had commented on the bradycardia occurring in cases of myxedema but had offered no extensive discussion of the cardiac changes.

However, in 1925, George Fahr presented the first comprehensive report of the condition in America in his article, "Myxedema heart."

August Krogh.

Monumental investigations dealing with the physiology of the capillary circulation were contributed by August Krogh (1874–), of Copenhagen. Krogh's investigations and publications have been extensive and have been so outstanding that in 1920 he received the Nobel Prize. In 1919 two important publications appeared, the first of which was titled, "The number and distribution of capillaries in muscles with calculations of the oxygen pressure head necessary for supplying the tissue." The summary of Krogh's article is as follows:

In striated muscles, the capillaries are arranged with such regularity along the muscle fibres that each capillary can be taken to supply a definite cylinder of tissue the average cross-section of which can be determined by counting the capillaries in a known area of the transverse section.

A formula is given which allows the calculation of the oxygen pressure head which is necessary and sufficient to supply the muscle with oxygen from the capillaries.

The mathematician Mr. J. Erlang has shown me the kindness to work out such a formula which runs

$$T_0 - T_x = \frac{p}{d}\left(\tfrac{1}{2} R^2 \log \text{nat} \frac{x}{r} - \frac{x^2 - r^2}{4}\right),$$

T_0 and T_x being the oxygen tensions in the capillary and the point x respectively. Putting $x = R$ and substituting ordinary logarithms for the natural we get the formula

transformed to $T_0 - T_r = \frac{p}{d}\left(1.15\ R^2 \log \frac{R}{r} - \frac{R^2 - r^2}{4}\right)$, which will give us the maximum tension difference necessary to supply the muscle with oxygen.

The number of capillaries per square mm. of the transverse section of striated

muscle appears to be a function of the intensity of the metabolism, being higher in small mammals than in larger forms.

The necessary oxygen pressure head deduced from the total number of capillaries is in all cases extremely low.

In a later publication in the same year Krogh produced the findings of other important experiments dealing with the physiology of the capillary circulation. This work was titled, "The supply of oxygen to the tissues and the regulation of the capillary circulation." His conclusions were as follows:

Microscopic observations, chiefly made by reflected light, are recorded to show that in the resting muscles of frogs and guinea-pigs most of the capillaries are in a state of contraction and closed to the passage of blood.

By tetanic stimulation of the muscles or by gentle massage a large number of capillaries are opened up. They can be observed to contract again afterwards. In spontaneously contracting muscles a large number of capillaries are likewise opened.

When the circulation is not extremely feeble (in the frog) the open capillaries are arranged at fairly regular intervals.

A method of *intra vitam* injection of india ink is described by which the capillaries which were open at the time become easily distinguishable in microscope slides prepared from the muscles.

The number of open capillaries per mm. of the muscular cross section has been counted in such preparations of resting and working muscles.

The average diameter of the open capillaries in resting muscles is much less than the dimensions of the red corpuscles which become greatly deformed during their passage. In working muscles the capillaries are somewhat wider.

The oxygen pressure head necessary for the supply of the tissue has been calculated from the countings and measurements for some typical cases. The oxygen pressure in resting muscles is, sometimes at least, very low, but in working muscles it approaches very near to that of the blood.

The evidence, showing that the capillaries are not merely passively dilated by blood pressure but constantly perform active changes in calibre, is discussed.

It is shown that clinical hyperaemia and anaemia are due mainly to changes in the calibre of capillaries and in the number of open capillaries.

Evidence is brought forward pointing to the arteriomotor and capillariomotor systems being able to act in opposite direction.

The inception of the modern use of mercurial diuretics in the treatment of cardiac edema had its origin in the work of P. Saxl (1880–1932) and R. Heilig, of Germany. In 1920, they reported on the favorable results obtained in the treatment of cardiac edema by the intravenous or intramuscular injection of the double salt of sodium mercurichlorphenyl oxyacetate with diethylbarbituric acid (novasurol). It contained 33.9 per cent of mercury and had been first introduced by Zieler in 1917, as an agent for the treatment of syphilis.

Saxl and Heilig found that the diuretic action of novasurol depended but little on the amount of water or sodium chloride in the blood, that the drug mobilized the water and sodium chloride in the edematous tissues and organs, and that atropine and large amounts of salt administered orally interfered with the diuretic action of the preparation. This work appeared in their article, "Ueber die diuretische Wirkung von Novasurol- und anderen Quecksilberinjektionen."

Sinee then an inereasing number of more refined and safer mercurial diuretics have been introdueed and this form of therapy has completely revolutionized the treatment of congestive heart failure. It has proved to be one of the greatest therapeutie innovations of all time.

The first report dealing with the surgical treatment of angina pectoris was that of Thomas Jonnesco (1860–1926), of France, who enthusiastieally proelaimed the curative effeets of cervical sympatheetomy. He performed his first operation in 1916, but the ease was not reported until 1920 under the title, "Angine de poitrine guérie par la résection du sympathique cervieo-thoraeique."

The patient forming the basis of Jonnesco's report was a man only thirty-eight years of age afflieted with syphilis. Both the heart and the aorta were enlarged and he had suffered from only five seizures of pain when operation was performed. Much doubt exists in our minds regarding the eorreet diagnosis in this case and it is not unlikely that the painful seizures were manifestations of syphilitie aortitis rather than of coronary disease. The patient's age and the existenee of syphilis tend to support this belief. Jonneseo also supported the idea that the anginal syndrome is due to irritation of the eardio-aortic plexus.

With the patient under loeal anesthesia, Jonneseo resected the left great sympathetic trunk from the base of the neek into the thorax ineluding the last two eervical ganglia and the first thoracic ganglion. This proeedure was earried out on the left side only and as the patient became completely relieved of his symptoms, he refused resection of the struetures on the right side.

This report was enthusiastieally reeeived by surgeons (not internists) throughout the world and many modifieations of the procedure were poured into the medical literature like an avalanche. This method of treatment proved not only hazardous but ineffeetive and gradually beeame abandoned. The various workers who became embroiled in this form of operative treatment are too numerous to mention in this volume.

While the recognition of ehanges in the T waves of the electroeardiogram associated with sudden obstruetion of the eoronary arteries had been mentioned by Herriek in 1919, the primary emphasis on these ehanges and their rather detailed deseription first oeeurred in the work of Harold Ensign Bennett Pardee (1886–   ), of New York. In 1920, in his article, "An eleetroeardiographie sign of coronary artery obstruetion," Pardee described the electrocardiographie findings in a patient observed four hours after the onset of the attack and in reeords obtained at later intervals. In the summary of his artiele, Pardee deseribed the changes observed in the electrocardiogram in the following manner.

6. The eharaeteristic ehanges appearing a day or two after the obstruetion are as follows: The QRS group is usually notehed in at least two leads, and usually shows left ventrieular predominance. The T wave does not start from the zero level of the reeord in either lead I or lead III though, perhaps, from a level not far

removed from it, and in this lead quickly turns away from its starting point in a sharp curve, without the short straight stretch which is so evident in normal records preceding the peak of the T wave. The T wave is usually of larger size than customary and accordingly shows a somewhat sharper peak. The T wave is usually turned downward in lead II and in one other lead. Not all of these changes are to be found in every record, but enough of them are present to give it a characteristic appearance.

7. It is concluded that this electrocardiographic sign indicates the presence of a rather large area of muscle degeneration, and when it is obtained from a patient who gives a history of precordial pain coming either in attacks or upon exertion, that it will complete the diagnosis of obstruction of a branch of a coronary artery.

8. It is suggested that this sign results only from a lesion within the area supplied by the left coronary artery, and that one within the area of the right coronary artery would cause changes so that the record would more or less closely resemble that which follows a lesion of the right branch of the auriculoventricular bundle.

Louis-Henri Vaquez.

In 1925 Pardee amplified these observations in his article, "Heart disease and abnormal electrocardiograms; with special reference to the coronary T wave."

The subsequent studies (beyond the scope of this quarter century) of Rothschild, Mann and Oppenheimer, Parkinson and Bedford, Barnes and Whitten, Wilson, Barnes and others have so thoroughly developed the electrocardiographic patterns of cardiac infarction that they are an integral part of present-day cardiology.

Even as late as 1921 the cause of angina pectoris continued to be a controversial issue. The prominent French cardiologist, Louis-Henri Vaquez (1860–1936), of Paris, still contended that the painful seizures are an expression of irritation of the cardio-aortic plexus. This view was expressed in his textbook, "Diseases of the heart," first published in 1921 and translated into English three years later. The views of Allbutt, Vaquez and others gave considerable impetus to the then much used surgical method of cervical sympathectomy.

In 1892, Vaquez described polycythemia vera, a disease also noted by Osler and which became known as "Vaquez-Osler disease."

Well remembered for his studies dealing with syphilis was Aldred Scott Warthin (1866–1931), of Ann Arbor, Michigan. A graduate of the University of Michigan in 1891, he became professor of pathology and director of the pathological laboratory at his alma mater in 1903.

Warthin was of the opinion that syphilis of the myocardium is of

common occurrence in spite of the contrary belief held by most pathologists. His demonstration of spirochetes in the myocardium of patients showing increases in interstitial fibrous tissue led him to identify the lesions as syphilitic. In 1925 Warthin brought forth the concept that syphilitic myocarditis could remain silent and latent for years and then suddenly result in death by virtue of an acute exacerbation or "crisis," as he called it. This work appeared in his article, "Sudden death due to exacerbation of latent syphilitic myocarditis."

Referring to the paradoxical views of others, Warthin caustically stated: "This is so contradictory to my own experience that I can only explain it on the ground of a failure of recognition and proper interpretation of myocardial lesions and a failure to demonstrate the association of spirochetes with such lesions."

Aldred Scott Warthin.

Warthin made important contributions to the pathology of the hemolymph glands and hematopoietic system and of mustard gas poisoning.

While the surgeons were engaged in performing various operations on the cervical and thoracic sympathetic nerves and ganglia, Felix Mandl (1892–), of Germany, introduced a more conservative method of treating angina pectoris. He reported temporary relief from the injection of procaine hydrochloride into the first five thoracic dorsal nerve roots. This report was published in 1925 as "Weitere Erfahrungen mit der paravertebralen Injektion bei der Angina pectoris."

This procedure was modified by others and in instances in which relief was obtained by the injection of procaine, absolute alcohol was later substituted following procaine anesthesia. This method of treatment is still occasionally employed in cases of refractory angina pectoris but usually as a last therapeutic resort.

SUMMARY

The first quarter of the twentieth century was one of outstanding achievement. Many of the uncertainties and much of the confusion regarding certain fundamental problems related to the heart and circulation became clarified. The true pattern of modern cardiologic concepts

came into being. It is not our intention to imply even remotely that at the time of this writing our so-called modern concepts will not be subject to drastic revisions. Mankind would justifiably be discouraged if further progress in the medical sciences could not be anticipated. The years from 1925 to the present have clearly removed any such misgivings.

One of the outstanding developments of this quarter century was the clarification and the unification of thought that occurred with regard to the coronary vessels and their diseases. While the modern ideas had been expressed by renowned predecessors no harmony of thought and opinion prevailed among learned physicians until the era was nearly completed.

The problem of the endocarditides became intelligible and the recognition of rheumatic endocarditis, acute and subacute bacterial endocarditis, and also the rarer forms, became almost routine procedures, not only on the part of the cardiologist but likewise on the part of the general practitioner of medicine.

A demand for diagnostic precision led to the establishment of a sound scheme of classification based on a purposeful nomenclature and such terms as "chronic myocarditis" and "mitral regurgitation" as primary cardiac diagnoses largely became abandoned. Vague diagnoses on the basis of ignorance and indifference were no longer condoned.

A clearer understanding of congenital cardiac anomalies was being gradually evolved, although much of this progress with regard to the medical profession at large occurred later.

Cardiovascular surgery made notable strides, even though the later years of the first quarter century and the early years of the second quarter century witnessed a surge of surgical experimentation which proved to be unscientific and virtually useless. However, both the surgeons and the cardiologists learned important lessons from the failures, so that the physicians of a later era, it is to be hoped, will not repeat these errors.

The introduction of quinidine and the mercurial diuretics was the therapeutic high light of the era. A better understanding of administration of digitalis became evident but even at this time much room for improvement is still apparent.

REFERENCES

Hall

°Hall, H. O.: The hallucinations of digitalis; does digitalis cause hallucinations, delirium or insanity under certain conditions? Am. Med. 1:598–600, 1901.

°Hall, H. O.: The delirium and hallucinations of digitalis. Am. Med. 9:489–490, 1905.

Matas

°Matas, Rudolph: Traumatic aneurism of the left brachial artery. Failure of direct and indirect pressure; ligation of the artery immediately above tumor; return of

pulsation on the tenth day; ligation immediately below tumor; failure to arrest pulsation; incision and partial excision of sac; recovery. M. News. 53:462–466, 1888.

°Matas, Rudolph: The treatment of abdominal aortic aneurism by a preliminary exploratory coeliotomy and peritoneal exclusion of the sac, followed at a later sitting by wiring and electrolysis, with the report of two hitherto unpublished cases. Tr. South. S. & Gynec. A. 13:272–330, 1900.

°Matas, Rudolph: Personal experiences in vascular surgery; a statistical synopsis. Ann. Surg. 112:802–839 (Nov.) 1940.

Brauer

°Brauer: Ueber chronische adhäsive Mediastino-Perikarditis und deren Behandlung. München. med. Wchnschr. 49:1072 (June 24) 1902.

°Brauer: Die Erfolge der Kardiolysis. München. med. Wchnschr. 49:1732 (Oct. 14) 1902.

°Brauer, L.: Die Kardiolysis und ihre Indicationen. Arch. f. klin. Chir. 71:258–267, 1903.

°Peterson: Quoted by Brauer, L.: Die Kardiolysis und ihre Indicationen. Verhandl. d. deutsch. Gesellsch. f. Chir. 32:80–89, 1903.

°Simon: Quoted by Brauer, L.: Die Kardiolysis und ihre Indicationen. Verhandl. d. deutsch. Gesellsch. f. Chir. 32:80–89, 1903.

White, P. D.: Heart disease. Ed. 3, New York, The Macmillan Company, 1944, pp. 664–665.

Moritz

°Moritz: Ueber orthodiagraphische Untersuchungen am Herzen. München. med. Wchnschr. 49:1–8 (Jan. 7) 1902.

Einthoven

°Einthoven, W.: Die galvanometrische Registrirung des menschlichen Elektrokardiogramms, zugleich eine Beurtheilung der Anwendung des Capillar-Elektrometers in der Physiologie. Pflüger's Arch. f. d. ges. Physiol. 99:472–480 (Nov. 3) 1903.

°Einthoven, W., Fahr, G. and de Waart, A.: Über die Richtung und die manifeste Grösse der Potentialschwankungen im menschlichen Herzen und über den Einfluss der Herzlage auf die Form des Elektrokardiogramms. Pflüger's Arch. f. d. ges. Physiol. 150:275–315 (Mar. 14) 1913.

Kristenson, Anders: Professor Willem Einthoven. Upsala läkaref. förh. 33:xi–xvi, 1928.

Leaman, W. G., Jr.: History of electrocardiography. Ann. M. Hist. n.s. 8:113–117 (Mar.) 1936.

Lewis, Thomas: Willem Einthoven. Professor of Physiology, University of Leyden. Heart. 14:v-viii (Aug. 1) 1928.

Obituary: Willem Einthoven (1860–1927); Dr. Med. Boston M. & S. J. 197:687–688, 1927.

Wenckebach: W. Einthoven. Deutsche med. Wchnschr. 2:2176 (Dec. 16) 1927.

Willius, F. A.: Professor W. Einthoven. (A memorial.) Mayo Clin. Bull. (Nov. 10) 1927, vol. 9.

Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors. St. Louis, C. V. Mosby Company, 1941, pp. 717–728.

Winterberg, H.: W. Einthoven. Wien. klin. Wchnschr. 40:1460 (Nov. 17) 1927.

Wenckebach

Falta, W.: K. F. Wenckebach zum Gedenken. Wien. klin. Wchnschr. 53:1067–1073 (Dec. 27) 1940.

Keith, Arthur: Professor K. F. Wenckebach. Lancet. 1:299 (Mar. 1) 1941.

Keys, T. E. and Willius, F. A.: Cardiac clinics. XCV. The achievements of Karel Frederik Wenckebach. Proc. Staff Meet., Mayo Clin. 17:332–336 (May 27) 1942.
Obituary: Prof. K. F. Wenckebach, M.D.; Hon. F.R.C.P. Brit. M. J. 1:219 (Feb. 8) 1941.
Ritchie, W. T.: Karel Frederik Wenckebach. Brit. Heart J. 3:141–144, 1941.
Scherf, David: Karel Frederik Wenckebach. Am. Heart J. 22:852–855 (Dec.) 1941.
*Wenckebach, K. F.: Ueber die Dauer der compensatorischen Pause nach Reizung der Vorkammer des Säugethierherzens. Arch. f. Anat. u. Physiol. (Physiol. Abtheilung). 1903, pp. 57–64.
*Wenckebach, K. F.: Beiträge zur Kenntnis der menschlichen Herztätigkeit. Arch. f. Anat. u. Physiol. (Physiol. Abtheilung). 1906, pp. 297–354.

Lenhartz

*Lenhartz, Hermann: Die septischen Erkrankungen. Wien, A. Hölder, 1903, 563 pp.

Hering

*Hering, H. E.: Analyse des Pulsus irregularis perpetuus. Prag. med. Wchnschr. 28:377–381, 1903.
Major, R. H.: Classic descriptions of disease; with biographical sketches of the authors. Ed. 2, Springfield, Illinois, Charles C Thomas, 1939, pp. 423–425.

Cloetta

*Cloetta, M.: Ueber den Einfluss der chronischen Digitalisbehandlung auf des normale und pathologische Herz. Arch. f. exper. Path. u. Pharmakol. 59:209–226 (Aug. 24) 1908.

Aschoff

*Aschoff, L.: Zur Myocarditisfrage. Verhandl. d. deutsch. path. Gesellsch. 8: 46–51, 1904.
Büchner, Franz: Ludwig Aschoff zum siebzigsten Geburtstage. Klin. Wchnschr. 15:1–2 (Jan. 4) 1936.
Dietrich, A.: Geschichte der Medizin, Lebensbilder. Ludwig Aschoff zum 70. Geburtstag. München. med. Wchnschr. 1:61–62 (Jan. 10) 1936.
Ernst, Paul: Ludwig Aschoff zum 60. Geburtstage; (10. Januar. 1926). Med. Klin. 1:79–80 (Jan. 8) 1926.
Koch, Walter: Ludwig Aschoff. (zum 10. Januar 1926.) München. med. Wchnschr. 1:74–75 (Jan. 8) 1926.
The Doctor's Page: Ludwig Aschoff. J. Organotherapy. 18:203–204, 1934.
Wätjen, J.: Ludwig Aschoff zum 70. Geburtstag. Deutsche med. Wchnschr. 1:79–80 (Jan. 10) 1936.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 729–739.

Tawara

*Tawara, S.: Das Reizleitungssystem des Säugetierherzens. Jena, Gustav Fischer, 1906, 200 pp.

Keith and Flack

Dedication: To Sir Arthur Keith—a beloved master of British anatomy. J. Anat. 69:1 (Oct.) 1934.
Kean, J. R.: Obituary: Martin Flack. Mil. Surgeon. 69:570 (Nov.) 1931.
"Keith, Sir Arthur," In Who's Who. *New York, The Macmillan Company,* 1940, p. 1729.
Keith, Sir Arthur. In The medical directory. London, J. & A. Churchill, Ltd., 1942, p. 834.

°Keith, Arthur and Flack, Martin: The form and nature of the muscular connections between the primary divisions of the vertebrate heart. J. Anat. 41:172–189 (Apr.) 1907.
Obituary: Martin William Flack, C. B. E., M. B. Oxf., director, Medical Research Department, R. A. F. Lancet. 2:430 (Aug. 22) 1931.
Obituary: Group Captain Martin Flack, C. B. E., M. A. Oxon., M. B., B. Ch. Oxon. Brit. M. J. 2:402–404 (Aug. 29) 1931.
Obituary: The late Group-Captain Martin Flack. Lancet. 2:510 (Aug. 29) 1931.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 741–762.

Mackenzie

°Mackenzie, James: Diseases of the heart. Ed. 3, London, Oxford University Press, 1914, 502 pp.
°Mackenzie, James: Principles of diagnosis and treatment in heart affections. London, Oxford University Press, 1916, 264 pp.
Waterston, David: Sir James Mackenzie's heart. Brit. Heart J. 1:237–248, 1939.
Willius, F. A.: Cardiac clinics. CXVI. The historic development of knowledge relating to the coronary circulation and its diseases: twentieth century to 1915. Proc. Staff Meet., Mayo Clin. 21:186–187 (May 1) 1946.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 763–800.
Wilson, R. M.: The beloved physician, Sir James Mackenzie. New York, The Macmillan Company, 1926, 316 pp.

Munro

Gross, R. E. and Hubbard, J. P.: Surgical ligation of a patent ductus arteriosus; report of first successful case. J.A.M.A. 112:729–731 (Feb. 25) 1939.
°Munro, J. C.: Surgery of the vascular system: I. Ligation of the ductus arteriosus. Ann. Surg. 46:335–338 (Sept.) 1907.

Thayer

Fishbein, Morris: A history of the American Medical Association. Philadelphia, W. B. Saunders Company, 1947, pp. 774–777.
Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, p. 632.
°Thayer, W. S.: On gonorrhoeal septicaemia and endocarditis. Am. J. M. Sc. n.s. 130:751–779, 1905.
°Thayer, W. S.: The early diastolic heart sound. M. Rec. 73:624 (Apr. 11) 1908.

Buerger

°Buerger, Leo: Thrombo-angiitis obliterans: a study of the vascular lesions leading to presenile spontaneous gangrene. Am. J. M. Sc. 136:567–580 (Oct.) 1908.

Abbott

°Abbott, Maude E.: Congenital cardiac disease. (Reprinted from Osler & McCrae's Modern Medicine, Ed. 2, 1915, vol. 4.) Philadelphia, Lea & Febiger, 1915, pp. 323–448.
°Abbott, Maude E.: Atlas of congenital cardiac disease. New York, The American Heart Association, 1936, 62 pp.

Hertz and Goodhart

°Hertz, A. F. and Goodhart, G. W.: The speed-limit of the human heart. Quart. J. Med. 2:213–218 (Jan.) 1909.

Ritchie

°Jolly, W. A. and Ritchie, W. T.: Auricular flutter and fibrillation. Heart. 2:177–221 (May 10) 1911.

°Ritchie, W. T.: Further observations on auricular flutter. Quart. J. Med. 7:1–12 (Oct.) 1913.

Rothberger and Winterberg

°Rothberger, C. J. and Winterberg, H.: Vorhofflimmern und Arhythmia perpetua. Wien. klin. Wchnschr. 22:839–844 (June 17) 1909.

Osler

Cushing, H. W.: The life of Sir William Osler. Oxford, The Clarendon Press, 1925, vols. 1 and 2, 1413 pp.

Memorial number of Canadian Medical Journal: Sir William Osler. The Canadian Medical Association Journal. (July) 1920, 123 pp.

°Osler, William: Lectures on angina pectoris and allied states. New York M. J. 64:249–256 (Aug. 22) 1896.

°Osler, William: Chronic infectious endocarditis. Quart. J. Med. 2:219–230 (Jan.) 1909.

°Osler, William: The principles and practice of medicine; designed for the use of practitioners and students of medicine. Ed. 7, New York, D. Appleton and Company, 1909, p. 839.

°Osler, William: The Lumleian lectures on angina pectoris. Lancet. 1:839–844 (Mar. 26) 1910.

Willius, F. A.: Cardiac clinics. CXV. The historic development of knowledge relating to the coronary circulation and its diseases: the nineteenth century. Proc. Staff Meet., Mayo Clin. 21:80–81 (Feb. 20) 1946.

Willius, F. A. and Keys, T. E.: Op. cit., pp. 801–811.

Rosenow

°Rosenow, E. C.: Immunological and experimental studies on pneumococcus and staphylococcus endocarditis (*"chronic septic endocarditis"*). J. Infect. Dis. 6:245–281 (Apr. 1) 1909.

°Rosenow, E. C.: On the mechanism of the production of infectious endocarditis. Tr. Chicago Path. Soc. 8:344–345 (Feb. 1) 1912.

Lewis

°Lewis, Thomas: Auricular fibrillation: a common clinical condition. Brit. M. J. 2:1528 (Nov. 27) 1909.

°Lewis, Thomas: Auricular fibrillation and its relationship to clinical irregularity of the heart. Heart. 1:306–372 (Mar. 30) 1910.

°Lewis, Thomas: The pacemaker of the mammalian heart as ascertained by electrocardiographic curves. J. Physiol. 41:ix–x (Nov. 19) 1910.

°Lewis, Thomas: Observations upon flutter and fibrillation. Part I.—The regularity of clinical auricular flutter. Heart. 7:127–130 (Apr.) 1920.

°Lewis, Thomas: Observations upon flutter and fibrillation. Part IV.—Impure flutter; theory of circus movement. Heart. 7:293–346 (Aug. 27) 1920.

°Lewis, Thomas: Observations upon flutter and fibrillation. Part IX.—The nature of auricular fibrillation as it occurs in patients. Heart. 8:193–228 (May) 1921.

°Lewis, Thomas and Cotton, T. F.: Observations upon flutter and fibrillation. Part V.—Certain effects of faradic stimulation of the auricle. Heart. 8:37–58 (Feb.) 1921.

°Lewis, Thomas, Drury, A. N. and Bulger, H. A.: Observations upon flutter and fibrillation. Part VI. The refractory period and rate of propagation in the auricle:

their relation to block in the auricular walls and to flutter, etc. Heart. 8:83–140 (May) 1921.
°Lewis, Thomas, Drury, A. N. and Bulger, H. A.: Observations upon flutter and fibrillation. Part VII.—The effects of vagal stimulation. Heart. 8:141–170 (May) 1921.
°Lewis, Thomas, Drury, A. N. and Iliescu, C. C.: A demonstration of circus movement in clinical flutter of the auricles. Heart. 8:341–360 (Aug.) 1921.
°Lewis, Thomas, Feil, H. S. and Stroud, W. D.: Observations upon flutter and fibrillation. Part II.—The nature of auricular flutter. Heart. 7:191–246 (Aug. 27) 1920.
°Lewis, Thomas, Feil, H. S. and Stroud, W. D.: Observations upon flutter and fibrillation. Part III.—Some effects of rhythmic stimulation of the auricle. Heart. 7:247–292 (Aug. 27) 1920.
White, P. D.: Thomas Lewis, 1881–1945. Am. Heart J. 29:419–420 (Apr.) 1945.

Libman

°Libman, E.: A case of embolic aneurisms. Proc. New York Path. Soc. n.s. 5:88–91, 1905.
°Libman, E.: The clinical features of cases of subacute bacterial endocarditis that have spontaneously become bacteria-free. Am. J. M. Sc. 146:625–645 (Nov.) 1913.
°Libman, E. and Celler, H. L.: The etiology of subacute infective endocarditis. Am. J. M. Sc. 140:516–527 (Oct.) 1910.
°Libman, Emanuel and Sacks, Benjamin: A hitherto undescribed form of valvular and mural endocarditis. Arch. Int. Med. 33:701–737 (June) 1924.

Schottmüller

°Schottmüller, H.: Endocarditis lenta. München. med. Wchnschr. 1:617–620 (Mar. 22) 1910.

Mall

Garrison, F. H.: Op. cit., p. 530.
°Mall, F. P.: On the muscular architecture of the ventricles of the human heart. Am. J. Anat. 11:211–266 (Mar.) 1911.

Herrick

°Herrick, J. B.: Clinical features of sudden obstruction of the coronary arteries. J.A.M.A. 59:2015–2020 (Dec. 7) 1912.
°Herrick, J. B.: Thrombosis of the coronary arteries. J.A.M.A. 72:387–390 (Feb. 8) 1919.
°Herrick, J. B.: A short history of cardiology. Springfield, Illinois, Charles C Thomas, 1942, 258 pp.
Holmes, W. H.: James Bryan Herrick; an appreciation. Privately printed, for The Central Interurban Clinical Club, (Nov.) 1935, 45 pp.
Willius, F. A. and Keys, T. E.: Op. cit., pp. 813–829.

Klotz

°Klotz, Oskar: Some points respecting the localization of syphilis upon the aorta. Am. J. M. Sc. 155:92–100 (Jan.) 1918.
°Klotz, Oskar and Manning, M. F.: Fatty streaks in the intima of arteries. J. Path. & Bact. 16:211–220 (Oct.) 1911.

Cabot

°Cabot, R. C.: Differential diagnosis; presented through an analysis of 385 cases. Ed. 2, Philadelphia, W. B. Saunders Company, 1912, 764 pp.
°Cabot, R. C.: The four common types of heart-disease; an analysis of six hundred cases. J.A.M.A. 63:1461–1463 (Oct. 24) 1914.

Starling

*Patterson, S. W., Piper, H. and Starling, E. H.: The regulation of the heart beat. J. Physiol. 48:465–513 (Oct. 23) 1914.

Allbutt

*Allbutt, Clifford: Diseases of the artéries including angina pectoris. London, Macmillan and Co., Limited, 1915, vol. 1, p. 373; vol. 2, pp. 4, 211 and 416.

Garrison, F. H.: Op. cit., p. 630.

Willius, F. A.: Op. cit. (Cardiac clinics. CXVI), pp. 187–188.

Cohn

*Cohn, A. E.: Clinical and electrocardiographic studies on the action of digitalis. (Abstr.) J.A.M.A. 64:463 (Jan. 30) 1915.

Plummer

*Plummer, H. S.: Blood-pressure and thyrotoxicosis. Tr. A. Am. Physicians. 30:450–457, 1915.

Robinson

Halsey, R. H.: A case of ventricular fibrillation. Heart. 6:67–76 (Apr. 30) 1915.

*Robinson, G. C.: A study with the electrocardiograph of the mode of death of the human heart. J. Exper. Med. 16:291–302 (Sept. 1) 1912.

*Robinson, G. C. and Bredeck, J. F.: Ventricular fibrillation in man with cardiac recovery. Arch. Int. Med. 20:725–738 (Nov.) 1917.

Willius, F. A.: Changes in the mechanism of the human heart preceding and during death. M. J. & Rec. 119 (Suppl.):xlix–liv (Mar. 19) 1924.

Zondek

Fahr, George: Myxedema heart. J.A.M.A. 84:345–349 (Jan. 31) 1925.

*Zondek, Hermann: Das Myxödemherz. München. med. Wchnschr. 2:1180–1182 (Oct. 22) 1918.

Krogh

*Krogh, August: The number and distribution of capillaries in muscles with calculations of the oxygen pressure head necessary for supplying the tissue. J. Physiol. 52:409–415 (May 20) 1919.

*Krogh, August: The supply of oxygen to the tissues and the regulation of the capillary circulation. J. Physiol. 52:457–474 (May 20) 1919.

Saxl and Heilig

*Saxl, Paul and Heilig, Robert: Ueber die diuretische Wirkung von Novasurol und anderen Quecksilberinjektionen. Wien. klin. Wchnschr. 33:943–944 (Oct. 21) 1920.

*Zieler, Karl: Novasurol, ein neues Quecksilbersalz zur Syphilisbehandlung, mit Bemerkungen über die Grundsätze der Quecksilberbehandlung. München. med. Wchnschr. 2:1257–1259 (Sept. 25) 1917.

Jonnesco

*Jonnesco, Thomas: II. Angine de poitrine guérie par la résection du sympathique cervico-thoracique. Bull. Acad. de méd., Paris. 84:93–102, 1920.

Pardee

*Pardee, H. E. B.: An electrocardiographic sign of coronary artery obstruction. Arch Int. Med. 26:244–257 (Aug.) 1920.

*Pardee, H. E. B.: Heart disease and abnormal electrocardiograms; with special reference to the coronary T wave. Am. J. M. Sc. 169:270-283 (Feb.) 1925.

Vaquez

Castiglioni, Arturo: A history of medicine. (Translated by E. B. Krumbhaar.) New York, Alfred A. Knopf, 1941, p. 798.
Garrison, F. H.: Op. cit., p. 618.
*Vaquez, Henri: Diseases of the heart. (Translated by G. F. Laidlaw.) Philadelphia, W. B. Saunders Company, 1924, 743 pp.

Warthin

Garrison, F. H.: Op. cit., p. 699.
*Warthin, A. S.: Sudden death due to exacerbation of latent syphilitic myocarditis. Am. Heart. J. 1:1-24 (Oct.) 1925.

Mandl

*Mandl, Felix: Weitere Erfahrungen mit der paravertebralen Injektion bei der Angina pectoris. Wien. klin. Wchnschr. 38:759-760 (July 2) 1925.

* Indicates original source consulted by the authors.

II

SPECIAL BIOGRAPHIES

HIPPOCRATES

(circa 460–circa 377 B.C.)

ALMOST EVERY statement regarding the life and works of Hippocrates has been questioned, if not contradicted. He has been venerated as the "Father of Medicine" and deified as the "Divine Hippocrates" (Appolonius); then again the very fact that such a person ever lived has been questioned and much doubt has been cast on the genuine authorship of the great collection of writings known as the "Hippocratic works." Jones spoke of "the shadowy Hippocrates of ancient tradition" and according to Sigerist "all that we certainly know of Hippocrates is that he lived . . ."

While we shall make no attempt to invent a biography for Hippocrates, it is contended that he was born about 460 B.C. on the Island of Cos in the Mediterranean. His father Heraclides was a physician. According to Galen, Hippocrates had two sons, Thessalus and Draco, both physicians, and each had a son named Hippocrates, which was also the name of the grandfather of Hippocrates. In accordance with this, the most famous ancient physician who bore the name of Hippocrates was Hippocrates II, the grandson of Hippocrates I. A son-in-law of our Hippocrates named Polybus is said to have been his most devoted follower and probably his successor in the teaching of the Hippocratic school of thought. References regarding the early life of Hippocrates are scanty and we know nothing except that he studied medicine under his father and Herodicus, the first Greek physician who is known to have cultivated the art of gymnastic exercises in the cure of disease. From the writings of his contemporaries we learn that Hippocrates was

a Coan, an Asclepiad (clan of hereditary physicians who claimed to be descended from Asclepius) and a professional trainer of medical students, and that he traveled far and wide (Plato in Protagoras and Phaedrus). According to Aristotle, another contemporary, he was already known as the "Great Hippocrates" during his own lifetime.

Of the circumstances connected further with his life, reliance has been placed on three ancient biographies, all of which were written long after his death. The first is by Soranus, who probably lived several centuries after Hippocrates; the second is by Suidas, a lexicographer of the eleventh century; and the third is by Tzetzes, a historian of the twelfth century.

Born as he was into a hereditary clan of physicians, Hippocrates had the advantage of ready access to collected observations of many generations as well as to one of the most eminent temples of health then in existence. It is to be noted further that the period during which he learned and practiced his profession with the greatest success and reputation coincided with a period during which Greek culture flourished to an extent unequaled in any other time. There were Pericles and Cimon among statesmen; Aeschylus, Sophocles, Euripides and Aristophanes among dramatists; Socrates, Aristotle, Plato, Democritus and Protagoras among philosophers; Herodotus, Thucydides and Xenophon among historians; Phidias, Polycletus and Praxiteles among sculptors. In this, the "Golden Age of Pericles," a school of thought was born which clearly separated medicine from priestcraft, pseudophilosophy and mysticism and established it as a science and an art; it raised medicine to the lofty ethical level exemplified by "The Oath." Without a doubt Hippocrates was the leading figure in this enlightening transformation. For cures sought from the gods by prayers or by incantations and charms he substituted the doctrine that "no one disease is either more divine or more human than another and none arises without a natural cause"; he believed that rational experience through methodical observation rather than through blind empiricism is the foundation of medical practice. So came into being bedside teaching, clinical case reporting and, incidentally, medical literature.

"Life is short, the art long, experience is fallacious, judgment difficult" expresses better than anything else the ardor toward perfection of knowledge concerning the nature of disease. The "Prognostics" and "Epidemics" provide evidence of painstaking observations regarding the natural course of disease at a time when the emphasis was on symptom complexes rather than on classified disease entities.

No one can furnish a bibliography, in the modern sense, of Hippocrates. A voluminous literature reflects the extensive research entered into by many historians who have made serious attempts to decide which, if any, of the Hippocratic works were written by Hippocrates

himself. Actually, as Edelstein has pointed out, "the solution of this problem does neither enhance nor deprecate Hippocrates' greatness, and importance." Certainly nothing worthy of the name of medicine existed before Hippocrates and in the century which followed his lifetime his teachings were held in high veneration. How much was added to them by his sons and disciples and to what extent they were later altered through confusion and error due to mistakes and ignorance, or perhaps even dishonesty of biographers, scribes and editors, we shall never know. It has been suggested by Singer that all kinds of sundry writings which could by any device be passed off as of Hippocratic origin were later added to what since has become the Hippocratic Collection. Shortly after 300 B.C. a group of these medical works were extensively circulated around the Alexandrian School of Medicine. Here it is said that they were codified and preserved. When the famous Library of Alexandria was destroyed, the collection no doubt went with it but by that time, many transcriptions had been made and spread throughout Europe. It is from these that we have our present knowledge of Hippocrates, both factual and legendary. In time these writings reached Galen, who arranged the Book of Aphorisms into seven sections, added his own commentaries and so enabled it to come down through the ages translated into Arabic, Italian, Spanish, French, Hebrew, English and German to be used as a textbook for the centuries that followed.

The collection as we know it today covers a wide range of topics but no attempt will be made to enumerate them nor do we intend to discuss their respective claim to genuine authorship. The ones most alluded to and quoted, "The aphorisms," are no doubt the conclusions written in his later years and based on earlier observations and writings such as "The prognostics," "The first and third epidemics," "On regimen in acute diseases," "On airs, waters, and places," "On wounds of the head," treatises which are accepted by the best authorities as being written by the great Hippocrates himself.

It is easy, even tempting, to read meanings into some of the suggestive passages in the writings of Hippocrates as reflecting a concise understanding of the medicine of today but the criticism can be upheld that many such passages are somewhat ambiguous and through their brevity even misleading. One might say of the style of Hippocrates that "the most obvious and characteristic of his peculiarities is an endeavor to express as much matter as possible in as few words as possible, to combine many thoughts into one, and always to leave the reader to supply something of his own." Be that as it may, the transcendent powers of observations contained in these writings can be denied by no one.

We wish to quote only a few such passages which bear on our subject of cardiovascular diseases.

Section 2, No. XLIV—"Those who are constitutionally very fat are

more apt to die quickly than those who are thin." We know that Hippocrates had no conception of the coronary circulation or its diseases; yet the effect of obesity on longevity and on sudden death must be admitted to be correct.

Section 6, No. VIII—"Sores on the body of dropsical persons are not easily healed."

Section 6, No. XIV—"In the case of a patient suffering from dropsy a flow of water by the veins into the belly removes the dropsy." The disappearance of edema from the extremities by shift of fluids into the abdomen when the patient assumes the recumbent position is a well-known phenomenon and Hippocrates accurately observed this, even though his ideas regarding the physiologic pathology of the condition were obviously incorrect.

Section 7, No. LVII—"There is no hope for a dropsical patient should he suffer a cough." This is the description of a patient dying of congestive heart failure, possibly complicated by pulmonary emboli. The sagacity of Hippocrates regarding the prognostic significance of clinical findings, even though their mechanism was not clear to him, is well illustrated here again.

Hippocrates lived to an advanced age but, since there is much uncertainty as to the time of his death, his age has been variously stated as eighty-five, ninety, 104 and 105 years. The latter part of his life was spent in Thessaly and he died in Larissa.

There are numerous interesting legends regarding the life of Hippocrates but they have been omitted because too much doubt has been cast on their authenticity. However, as Francis Adams has it, "What more, in general, can we desire to know respecting the biography of a physician than the manner in which he was educated, how he was esteemed by his contemporaries, and what he did and wrote to reflect credit on his profession? The approbation and gratitude of those who have consulted him for the cure of their maladies are the best testimony to the public character of a physician, and the estimation in which his writings are held by those members of his own profession is what constitutes his professional reputation. I need scarcely say that, as a medical author, the name of Hippocrates stands pre-eminently illustrious. In this way he has left monuments of his genius more durable than the statues of Phidias, his contemporary, and as enduring as the tragedies of Sophocles, or the *Olympiac* odes of Pindar."

REFERENCES

Adams, Francis (translator): The genuine works of Hippocrates. London, The Sydenham Society, 1849, vol. 1, pp. 3–130.

Adams, Francis (translator): The genuine works of Hippocrates. London, The Sydenham Society, 1849, vol. 2, pp. 683–774.

Dock, G.: First aphorism of Hippocrates. Ann. Int. Med. 6:129–142 (July) 1932

Duncan, J. M.: The father of medicine. Edinburgh M. J. 22:481–499, 1876.
Edelstein, Ludwig: Notes and comments: The genuine works of Hippocrates. Bull. Hist. Med. 7:236–248 (Feb.) 1939.
Jones, W. H. S. (translator): Hippocrates. London, William Heinemann, Ltd., 1931, vol. 4, pp. 99–221.
Lorimer, G.: An address on medicine in ancient Greece: the methods of Hippocrates and work accomplished by him. Brit. M. J. 2:196–199 (July 27) 1907.
Lund, F. B.: The life and writing of Hippocrates; a sketch. Boston M. & S. J. 191: 1009–1014 (Nov. 27) 1924.
Major, R. H.: Hippocrates and the Island of Cos. Yale J. Biol. 14:1–11 (Oct.) 1941.
Shastid, T. H.: Hippocrates, father of modern medicine. M. Pickwick. 5:3–12, 1919.
Sigerist, H. E.: The great doctors; a biographical history of medicine. (Translated by Eden and Cedar Paul.) New York, W. W. Norton & Company, Inc., 1933, p. 36.
Singer, Charles: Hippocrates and the Hippocratic collection. In: The Encyclopaedia Britannica, Ed. 14, London, The Encyclopaedia Britannica Company, Ltd., vol. 11, pp. 584–585.

IBN AN–NAFIS

(circa 1210–1288)

IBN AN-NAFIS, or more fully Alā ad-Din ibn an-Nafis al-Qurashi ad-Dimashqi, was born about the year 1210. Until very recent years little was known of this famous Arabian physician or his works. Credit for the historic rediscovery of Ibn an-Nafis belongs to a young Egyptian physician, Muhyi ad-Din at-Tatāwi, who presented a thesis for his doctorate degree before the Medical Faculty of Freiburg in 1924. The subject of his thesis was the discovery of the pulmonary circulation by Ibn an-Nafis. However, Tatāwi's thesis was not published, and if his work had not stimulated the interest of others who learned of this study, the available facts regarding Ibn an-Nafis and his monumental contribution might still be hidden in obscurity.

Meyerhof, in 1933, from his own biographic researches, those of Tatāwi and those of others, has interestingly revealed the facts that are known about Ibn an-Nafis, his life and his works. Meyerhof stated that he was able to find nine biographies of Ibn an-Nafis, three of which were written in French. They were all brief, except two, and these were almost identical. These latter biographies had never been published. Ibn Fadlallāh al-'Umari, who died in the great plague of Damascus in 1348, was the author of one and the celebrated Arabian historian, Khalil ibn Aibak as-Safadi, a contemporary of the former, was the author of the second biography. From these two accounts the basic information regarding Ibn an-Nafis was obtained.

No information is available regarding his parents, childhood or early education. Ibn an-Nafis was reared in Damascus and studied the medical sciences under Muhadhdhib ad-Din ad-Dakhwār. Ad-Dakhwār was a

brilliant scholar and able teacher. The biographies indicate that Ibn an-Nafis was a master of the art of healing and that he had no peer in the acuity of his investigations.

He was a tall man of slender stature, dignified, austere and refined. Special comment was made regarding his polite manners. Ibn an-Nafis did not marry; however, he built a beautiful home in Cairo, with marble floors. He apparently spent much time in his library and was a prolific writer, rarely consulting books. Pens (quills) were cut for him and once engaged in writing he would discard a blunt quill, pick up another and proceed without any delay.

Ibn an-Nafis' writings were not confined to medicine; he also wrote on logic, philosophy, theology, jurisprudence, applied law, the Arabic language, tradition and rhetoric. It appears that he did not excel in these subjects; yet he contributed to them in some degree. Ibn an-Nafis wrote numerous commentaries on the writings of others. He wrote a commentary on Hippocrates' "Aphorisms," his "Prognostics" and his "Epidemics," as well as on Galen's "Anatomy." The most significant commentary written by Ibn an-Nafis concerned Avicenna's "Anatomy." This work will be considered more fully later, as it concerned Ibn an-Nafis' great contribution to the knowledge of the heart and circulation.

He wrote three original books relating to medicine. "The comprehensive book on medicine" (Kitāb ash-Shāmil fi't-Tibb) was an enormous encyclopedic work which was never completed. No copy of this work is known to exist today although a manuscript was known to have existed in Cairo about the middle of the fourteenth century. Another work, "The well-arranged book on ophthalmology" (Kitāb al-Muhadhdhab fi'l-Kuhl), is also nonexistent, but references to it were found in later works on the subject. The final book, "The choice of aliments" (Kitāb al Mukhtār min al-Aghdhiya), appeared to be of relatively little importance. A manuscript of this work was in the Berlin State Library.

Ibn an-Nafis' commentary on Avicenna's (Ibn Sînâ) "Anatomy" is historically his most important contribution because it contained the first description of the pulmonary circulation. The exact time of its inscription is not known but Meyerhof believes it to have been about the middle of the thirteenth century. The commentary was a voluminous work. At least four manuscripts of it have been preserved. In the preface of Ibn an-Nafis' work he clearly stated that the prevailing religious laws and his own natural charity had prevented him from performing anatomic dissections. Therefore, he was obliged to study the form of the viscera from the works of others, especially those of Galen.

According to these admissions it is evident that Ibn an-Nafis utilized speculation and logic in correctly deducing the general scheme of the pulmonary circulation, accepting some of Galen's tenets while deliberately discarding others. He correctly conceived the general prin-

ciples of respiration and deduced the fact that the blood comes to the lungs from the right side of the heart and after becoming aerated in the lungs, returns to the left chambers of the heart. Ibn an-Nafis insisted that the thick interventricular septum is impervious and does not contain the "invisible pores" of Galen. No doubt can exist that this illustrious Arabian had correctly conceived the pulmonary circulation and its essential functions.

The discovery of the lesser circulation has been universally credited to Servetus. In view of the fact that Ibn an-Nafis' contribution was recorded in a foreign and uncommon language, and remained relatively obscure and local even in the succeeding centuries, there can be little doubt that Servetus and his contemporaries were completely unaware of its existence. The earlier exposition of the pulmonary circulation by Ibn an-Nafis (approximately three hundred years before) in no manner detracts from the importance and originality of Servetus' work. In fact, until very recent years, the basic concept of the pulmonary circulation in medical knowledge was solely vested in Servetus' contribution.

The biography of Ibn an-Nafis also contains an interesting account of his spontaneity and profound processes of thought. One day, while at a public bath, he abruptly went to the dressing room, demanded writing material and inscribed a long treatise on the pulse. According to his students, Ibn an-Nafis was a master in the theory of medicine but did not excel in its practice. He was reluctant to prescribe remedies as long as he could apply dietary measures and did not order compound remedies when simple ones could be used. One day the druggist became infuriated at Ibn an-Nafis because of his therapeutic philosophy and said to him, "If you intend going on with prescriptions of this kind, you had better go and sit in a butcher's shop! So long as you are with me, please prescribe sugar, syrup and remedies only!"

Ibn an-Nafis lived a long and useful life, attaining the age of nearly eighty years. The nature of his final illness is not known but during this illness some of his physician friends prescribed wine for him. He refused to take this, however, with the comment, "I do not like to present myself before Allah, the Most High, with wine in my body." He was ill for six days and passed away on a Friday morning in the year 1288.

Ibn an-Nafis bequeathed his library to the Mansoury (Mansūri) Hospital, in which institution he had held the position of Dean.

REFERENCES

Haddad, S. I. and Khairallah, A. A.: A forgotten chapter in the history of the circulation of the blood. Ann. Surg. 104:1–8 (July) 1936.

Meyerhof, Max: Ibn An-Nafis (XIIIth cent.) and his theory of the lesser circulation. Isis. 23:100–120, 1935.

Temkin, Owsei: *Was Servetus influenced by Ibn an-Nafis? Bull. Hist. Med. 8*:731–734, 1940.

MICHAEL SERVETUS

(1509–1553)

The sixteenth century recorded numerous tragedies in Europe, many of which resulted from the enduring influences of the Inquisition. To be a heretic or to be guilty of any offense against the orthodox church was a crime often punishable by death. It was the misfortune of Michael Servetus to be born at a time when Europe was dominated by an unenlightened clergy, some of whom deliberately discouraged scientific progress, quashed original thinking and prohibited the expression of unorthodox opinion. Living in a later era of civilization this same man might have been a hero instead of a martyr.

Michael Servetus, also known as Michel Villeneuve and Michael Servetus Villanovanus, was born in 1509 at Villanueva de Sigena in the province of Huesca in Spain. His parents were respected citizens in good circumstances and of Catholic faith. This latter fact is of singular importance as the story of young Michael unfolds.

The belief exists that the early education of Servetus was acquired in a nearby convent school and that later he attended the neighboring University of Saragossa. It is probable that he first undertook the study for the priesthood. He was an unusually apt student and without a doubt, a precocious young lad. Servetus, however, did not become a priest, as the next record of his education found him at Toulouse, studying canon and civil law.

At about the age of twenty years, Servetus entered the service of the Friar Quintana, confessor of the Emperor Charles V, in the capacity of private secretary. In the retinue of the Emperor he went to Italy and, while there, was a spectator at a religious ritual of humiliation which

he interpreted as a material and mercenary exhibition unbecoming to his concept of true religion. This spectacle so disgusted young Servetus that he developed a violent hatred of his inherited religion. The sparks of this hatred kindled a flame which ever burned more brightly in the ensuing years and, without a doubt, charted the course of his future destinies.

While at Toulouse, Servetus had close contacts with young men who had become deeply interested in the new religious ideas of Martin Luther, the celebrated German religious reformer. In many quarters evidences of dissatisfaction with the established religious order became apparent and various persons became actively engaged in bringing about reforms. It thus appears perfectly natural that young Servetus, already opposed to the existent religious precepts and rituals, should eagerly embrace a new order of thought and faith. When he was only twenty-one years of age, the Emperor attended the Diet of Augsburg, where the Princes succeeded in bringing about the political recognition of Protestantism. Even at this early age, Servetus possessed mature views regarding religion and the controversial issues of the times. He recorded his opinion in the following words: "For my own part, I neither agree nor disagree in every particular with either Catholic or Reformer. Both of them seem to me to have something of truth and something of error in their views; and whilst each sees the other's shortcomings, neither sees his own. God in his goodness give us all to understand our errors, and incline us to put them away. It would be easy enough, indeed, to judge dispassionately of everything, were we but suffered without molestation by the churches freely to speak our minds."

Servetus remained in the service of Quintana for about a year and a half and it was probably with a sigh of relief that the Friar saw him depart. He next journeyed to Germany in order to become acquainted with those religious leaders interested in the Reformation. His reception at first was cordial but as discussion became more extended, it was not long before the Reformers were astounded by the antitrinitarian doctrines expressed by this young upstart. Wherever he went, rebukes concerning his presumed heretic remarks were heaped on him. In spite of his youth and public obscurity, Servetus clearly displayed unswerving courage and determination in behalf of his beliefs when he refused to be throttled by his elders. He finally decided to place the issue frankly before the people by writing and publishing a small volume discussing doctrines, entitled "The errors of the Trinity." Interestingly, this volume appeared without the name of the printer but the name, "Michael Serveto *alias* Reves ab Aragonia, Hispanum, MDXXXI" appeared on the title page. He hoped that his doctrines would be favorably received by the more liberal Swiss Reformers but in this he was disappointed, for they were shocked by what they termed blatant blasphemies. Like-

wise in Strasbourg his writings were disclaimed and one cleric remarked that the author of such trash should be disemboweled and torn to pieces.

In fairness to young Servetus it is important to understand his belief in terms of present-day religious philosophy. This is available through the researches of Professor Emerton, quoted by Cumston.

> He would not admit that the eternal Son of God was to appear as man, but only that a man was to come who should be the Son of God. This is the earliest intimation we have as to the speculations which were occupying the mind of the young scholar. It is highly significant that from the start he was impressed with what we should now call the historical view of theology. As he read the Old Testament, its writers seemed to him to be referring to things that their hearers would understand. Their gaze into the future was limited by the fortunes of the people at the moment. To imagine them possessed of all the divine mysteries, and to have in mind the person of the man Jesus as the ultimate object of all their prophetic vision, was to reflect back the knowledge of history into a past to which such knowledge was impossible. So far as I can understand, this is the key to all of Servetus' later thought. . . . To his contemporaries he was a half-mad fanatic; to those who have studied him, even sympathetically, his thought remains to a great extent enigmatical; but this one point is fairly clear: that he grasped, as no one up to his time had grasped, this one central notion, that, whatever the divine plan may have been, it must be revealed by the long, slow movement of history—that, to understand the record of the past, it must be read, so far as that is possible with the mind of those to whom it was immediately addressed, and must not be twisted into the meanings that may suit the fancy of later generations.

A year after the publication of his first book (1532) Servetus circulated another little book featuring two dialogues, one explanatory and the other conciliatory, but this effort was also in vain, for it heaped fuel on an already brightly burning fire. The reaction among the Protestants was violent and Servetus realized the importance of absenting himself from his critics. He went to Paris, adopted the name of Michel Villeneuve or Michael Villanovanus and during the ensuing twenty-one years engaged in numerous undertakings. They comprised further study, lecturing, practicing medicine and continuing his writing. He was still possessed of a fervent hope that the world might be reformed if he could but restore to the people the primitive doctrine of religion.

Little is known regarding Servetus' early years in Paris. It is possible that he secured employment as a teacher and established contacts with printers by whom his linguistic accomplishments would be in great demand. At this stage of his career, he first met Calvin, also a young student, engrossed in religious studies. How strange that these two young men, both possessed of certain religious ideals, both seeking deliverance from the faith of their forefathers, should seek their objectives in such divergent philosophies! Little did they realize that the destinies of each would ultimately be evolved from this seemingly innocent association. It is natural to conclude that they had frequent discussions dealing with religion and in view of Servetus' contacts with the elder German and Swiss Reformers it is not difficult to understand that Servetus and Calvin

were soon at swords' points. For the time being, however, their disagreements remained a private matter but the seed of violent opposition was already growing in Calvin's consciousness, only to mature when Servetus persisted in annoying him.

In 1534, after a brief sojourn in Avignon and Orleans, Servetus journeyed to Lyons, where he entered the employ of the brothers Trechsels, the celebrated printers. Editing, proofreading and perhaps translating works comprised his duties. A year later he published a remarkable folio of Ptolemy's "Geography" with remarks and discussions regarding the various countries included, revealing his wide scope of knowledge. However, his comments were colored by his personal prejudices in such blunt language as to provoke unfavorable criticism and require revisions in the second edition of the work. One of the chief criticisms was of the description of Palestine. Servetus asserted that it was anything but a "Promised Land," that instead of flowing with milk and honey and being a land of olives, corn and vineyards, it was barren, and the tales regarding its productiveness were but boastful and untrue statements.

Although no written document exists, it has been suggested that Servetus and Rabelais, the great French humorist, physician and so-called archheretic, became acquainted at Lyons. However this may be, it seems that the celebrated physician, Symphorien Champier, one of the most distinguished humanists of the sixteenth century, exerted a strong influence on Servetus in his decision to study medicine. Servetus assisted this notable in the writing of his "French Pharmacopoeia." Champier was a learned man, a Galenist, a historian of note, and founder of the hospital and medical school at Lyons. Champier without a doubt gave Servetus his first instruction in medical matters as well as interesting him in astrology, a side line to various sciences popular in that era. When Fuchsius, the distinguished professor of medicine at Tübingen, Germany, attacked Champier for his astrologic beliefs, Servetus defended his preceptor by issuing a little pamphlet.

Servetus then returned to Paris where he began the earnest study of medicine, first at the College of Calvi and later at the College of the Lombards. He had apparently saved sufficient funds from his earnings at literary tasks to pursue this phase of his education comfortably. Not much is known of his years as a medical student except that he came under the influence of three celebrated physicians, Guinther, Jacobus Sylvius and Vesalius. Servetus later stated that with the help of these men he examined the entire human body and demonstrated to the students all the muscles, veins, arteries and nerves. Vesalius was an anatomic genius, who, however, confused human and animal anatomy. It was from him that Servetus learned the fundamentals of this science which later enabled him to make an important medical contribution.

Servetus, like his preceptor, Champier, dabbled in astrology. Many intellectuals of the sixteenth century literally lived and worked under the influence of the stars. Astrology was forbidden by the Church, although it was taught in some universities and was practiced by many reputable physicians. The Paris Faculty forbade lectures on the subject although the King himself was interested in astrology and went so far as to employ a professional astrologer, named Thibault. Servetus, although fully aware of the scholastic ban on astrology, instituted a course of lectures on the subject soon after his arrival in Paris. Here he again demonstrated the courage of his convictions. It was not long, however, before he clashed with the authorities.

To make matters worse, Servetus, under the guise of an apology, printed a statement attacking the doctors and asserted that wars, pests and all the affairs of mankind depend on the heavens and the stars. The Dean of the Faculty upon hearing of this so-called apology attempted to dissuade Servetus from circulating the pamphlet and, meeting him one day as he was leaving the school, accosted him and brought the matter to his attention. Several people were present at this chance meeting. Servetus, in his extraordinary independent manner, not only refused to comply with the Dean's request but loosed a tirade of wrath against his superior.

The pamphlet of eight pages which caused such a commotion contained references from the works of such notables as Plato, Aristotle, Hippocrates and Galen, which were selected to support his own contentions. In his statements vindicating astrology, Servetus not only included the tenets of others but recorded his own observations. He spoke of an eclipse of the moon by Mars, predicted weather conditions, discussed the influence of the moon in determining critical days of diseases, and asserted that Galen's beliefs should be inscribed in gold.

It appears that the Faculty encountered considerable difficulty in persuading the authorities to prosecute Servetus. This was probably occasioned by the influence of the King's astrologer, Thibault. It was not until considerable pressure was brought to bear on the Theological Faculty and the Congregation of the University that the issue was brought before Parliament. The decision of the Parliament was somewhat of a compromise. It demanded the recall of the pamphlet, booksellers were prohibited from retaining any copies in their possession, lectures on astrology were banned and Servetus was admonished to treat the Faculty with decorum and respect. In turn, the Parliament requested leniency on the part of the Faculty and suggested that they deal with the offender in a parental manner. The trial ended in March, 1537.

Servetus had been interested in medical matters but a short time when he published his first contribution in this field. The influence of his preceptor, Champier, came to light again. The little volume which

Servetus compiled dealt with syrups and their uses. Interspersed among the purely technical phases of the work are certain expressions dealing with his philosophy of disease. A significant statement indicates his mature and advanced process of thought: "Diseases are only perversions of natural functions and not new entities introduced into the body." That this volume met with popular approval is evidenced by the fact that it was reprinted twice in Venice in 1545 and 1548, and twice in Lyons, in 1546 and 1547.

Servetus left Paris in 1538 and began the practice of medicine in Charlieu, a small community not far from Lyons. He spent less than a year in this locale. He was, without a doubt, a restless soul, for history records an ever-increasing list of visitations, motivated in part by his own free will and in part by the violent opposition of the increasing number of his antagonists. One of his few remaining friends among the clergy, Pierre Pammier, the Archbishop of Vienne, induced him to locate in Vienne and become his personal physician. This invitation was accepted and undoubtedly Servetus realized that at last a haven of refuge was afforded him under the sheltering arms of the Archbishop. How this strange companionship endured is difficult to understand and indeed the Archbishop's act stamped him as a broad-minded and tolerant man who refused to accept the narrow, bigoted philosophy of a religion which so universally dominated that era. Servetus spent the ensuing fourteen years in the practice of medicine.

Servetus maintained contacts with the printers, the Trechsels, who in the meantime had opened a printing establishment in Vienne. In 1541 he was responsible for a new edition of Ptolemy's "Geography," which was dedicated to his friend and benefactor, the Archbishop. In this edition, he deleted many anticlerical remarks that had appeared in the first edition, without a doubt owing to his desire to remain in the good graces of Pammier and his associates. However, testifying to the fact that Servetus was still interested in religious matters, in the following year he published an edition of Pagnini's Bible. He was frankly outspoken in his religious beliefs and interpretations but strangely enough, his comments neither weakened nor strengthened his position in the community. He also edited a series of educational works for Frelon, a publisher in Lyons, and through this enterprise he again came in contact with Calvin. now in Geneva.

Servetus was not irreligious, as some might be led to believe. He was an idealist conscientiously opposed to the existing doctrines of the Church. Furthermore, he was a dreamer and a mystic possessed of extraordinary enthusiasm which on many occasions prodded him to precipitate action when contemplative deliberation would have dictated a more conservative course. He was obsessed by the conviction that a drastic revision of the doctrines of religion could restore a simple

and sincere Christianity to a confused and spiritually hungry world. Not content with submission and perhaps encouraged by the rather passive attitude of the clergy to his latest publications, he provoked new and more bitter antagonisms by entering into correspondence with Calvin. He attacked the sacraments in a manner that shocked Calvin and incited his indignation to a fever pitch.

For a number of years Servetus had been preparing a work in which he hoped it would be possible to restore primitive Christianity to the people. He sent some of the manuscript to Calvin, whose denunciation of the subject matter and of the author became violent. Calvin complained to Pastor Farel in the following words: "Servetus has sent me an enormous volume of his reveries, at this time advising me with fabulous brasenness that I would therein find unheard-of marvels. He offers to come here [to Geneva] if agreeable to me, but I do not wish to give my word, because, if he came I would not suffer him to leave alive if my authority has any power." How contrasting were the religious ethics of the sixteenth century from those of today! What devout cleric of modern times would dare record a threat of that type?

This large volume, titled "Restitutio Christianismi," was published in 1553. After numerous attempts to secure a printer to undertake this dangerous project, Servetus finally induced a local printer to accept the work. A press was set up in a small house under very secret conditions and 1,000 copies appeared in the course of a few months. The title page of the volume bore only the name of the book and the date. On the last page were the initials of Servetus' name, M.S.V. The volume revealed no clue as to the identity of the printer.

The major theme of this work was essentially a disquisition on his religious philosophy. Servetus entered into obscure discussions regarding the Trinity and infant baptism. In reality, the book dealt with a complete plan for the reformation of religion rather than with heretical insinuations. Any departure from the generally accepted orthodox doctrines was at the time labeled heresy. The theme of zealous pantheism which dominated the entire manuscript shocked the Christians because it was directed to the reform of orthodoxy.

This volume also contained Servetus' only significant contribution to medicine. Here he described the pulmonary circulation. He demonstrated the circulation of the blood from the right side of the heart through the vessels of the lungs where it was mixed with the air and thence back to the left side of the heart. The fallacious tenets of Galen were still generally accepted at this time.

Servetus did not appreciate the importance of his discovery because he was so absorbed in religious philosophy that he used it only to illustrate a point in discussing the nature of the Holy Spirit. Copies of the "Restitutio Christianismi" were ordered to be burned at the time that

Servetus met death on the pyre. Only two copies of the work were known to have escaped destruction and they were later discovered in Vienna and Paris. A rare reprint was published in Nuremberg in 1790.

While Ibn an-Nafis, who lived in the thirteenth century, is the first person known to have reasoned the concept of the pulmonary circulation and described it, his work remained obscure until recent years. It can be justly assumed that Servetus knew nothing of Ibn an-Nafis' work and therefore both descriptions of the pulmonary circulation were without a doubt original.

"Restitutio Christianismi" had barely been issued from the press when a great commotion occurred among the clergy and particularly among the Reformers. Among the French refugees in Geneva who formed Calvin's party was a man from Lyons, Guillaume Trie or de Trie, who because of religious zeal and certain misconduct had been banished from his home and had eagerly embraced the refuge and religion of the Reformers. He, however, carried on a correspondence with a relative in Lyons, Antoine Arneys. Arneys, a devout Catholic, was greatly perturbed by the heresy of his relative and undertook in a most determined manner to bring Trie back into the fold. Calvin, who was a shrewd opportunist, foresaw the possibility of using these recruits to serve his own purpose. Having possession of the manuscript which Servetus had sent him he had no difficulty in identifying it as part of the notorious volume, which bore no signature. At Calvin's direction, Antoine Arneys denounced the book to the Inquisition of Lyons, proclaimed the identity of the author and exhibited the index and the first four pages of "Restitutio Christianismi."

Cardinal de Tournon, governor as well as Archbishop of Lyons at this time, was a violent antagonist of heretics and eagerly undertook the task of bringing Servetus within the clutches of the law. In order to strengthen his authority, the Cardinal petitioned Rome to send a relentless inquisitor, Father Mathieu Ory, to conduct the proceedings. This man held the awesome title of penitentiary of the Pope and general inquisitor of the kingdom of France and of all the Gauls. Together, the Cardinal and Father Ory commanded the Lieutenant-General of the King, Monsieur de Mangiron, to arrest Michael Servetus. Servetus appeared before the Lieutenant-General and, attempting to disprove the accusations, requested that his house be searched. This request was granted but no incriminating evidence was detected. A printing establishment under suspicion was also investigated, and although all the employees were carefully questioned, none would admit that they had participated in the printing of the book.

Because of lack of evidence the proceedings were officially closed but the inquisitors quietly continued their investigation. Father Mathieu Ory communicated with Antoine Arneys, submitting a letter intended

for Guillaume Trie, commanding him to send the entire book instead of a few pages. Trie did not comply with this order, convinced that Servetus and the printers could as well deny any knowledge of the entire book as of the few pages. He, however, did send the letters which Servetus had written to Calvin. These letters contained the same expressions as occurred in the book and, being in Servetus' handwriting, could not readily be denied.

Servetus' arrest was accomplished by trickery. He was requested to administer medical aid to several inmates of the city prison and unsuspectingly fell into the trap so subtly set for him. A carefully planned scheme of incrimination was now undertaken. He was shown a few lines of his own handwriting and readily admitted that he had written them, not suspecting that on the following day, the bundle of letters he had written to Calvin would be presented to him for identification. Servetus remained in prison only a few days, for he escaped through the garden, unquestionably aided by some individual of prominence, who had been his patient and friend. In spite of his escape, the trial was continued and culminated in the pronouncement of the penalty of death. In the meantime, Servetus had wandered to the French border where immediate departure from the country would be only a question of minutes.

After reaching the decision to leave France, Servetus was undecided where he should seek refuge. His first impulse was to return to his native Spain. This idea was abandoned and in turn he considered Germany and Italy. Servetus finally decided to go to Italy where, he believed, his religious ideas would meet with less antagonism than in other countries. Regrettably, he chose to travel to Italy by way of Switzerland. He reached Geneva on July 17, 1553. He managed to remain in obscurity for three weeks and he might have permanently escaped detection had he not become obsessed with the idea of attending one of Calvin's sermons. It is possible that he attended this gathering with the deliberate intention of picking a quarrel with Calvin. Servetus had never relinquished the desire to engage Calvin in public debate and at this stage of events Calvin himself was in a somewhat precarious position, having acquired numerous enemies and antagonists.

Calvin soon learned of Servetus' presence in Geneva and lost no time in bringing about his arrest and imprisonment. The existing law of Geneva pertaining to arrests based on accusations contained a most unusual provision: the accuser, regardless of the nature of the accusation, was to be placed in prison with the accused in order that he might suffer the same punishment in event that the accusation was false. However, this law was not unequivocally enforced, and Calvin contended that his time was so valuable and his duties were so urgent that he could not possibly submit to this edict. Instead, his secretary, Nicolas Delafontaine,

was permitted to serve in Calvin's place. The trial began immediately and was continued for two months.

In order to facilitate the procedure, Calvin abstracted the contents of Servetus' books and manuscripts to form the basis of the inquiry. Servetus requested that the trial be made a public one but his request was not granted. Berthelier, the son of Geneva's heroic liberator and the leader of the anti-Calvinistic party, attempted to defend Servetus but to no avail. The trial was ridiculous, prejudiced and utterly unfair. The life of a human being was being contested on the bigoted interpretation of vague differences of scholastic religious philosophies. Among the long list of presumed heresies laid at the feet of Servetus was but one which was valid even in the sixteenth century. Calvin pounced on this issue like a beast on its prey with the result that the main theme of the trial became focused on Servetus' pantheistic views.

On August 21, the Lower Council decreed that the case was important to all Christianity and because of its significance should be removed from the lower court to Vienne. It was further decided to seek additional evidence in Vienne and to learn the opinions of other Swiss churches. These inquiries resulted only in vague pronouncements which in no manner deterred the benighted theologians from pursuing their preconceived and vindictive scheme. Servetus was patient and courteous throughout the entire trial but resolutely refused to deny any of his convictions. It is evident that not all shared Calvin's views because some members of the Council believed it was altogether too serious a decision to condemn a man to death on the basis of his beliefs alone. Then additional complaints were introduced by the Calvinists to the effect that Servetus had attempted to disturb the peace of Geneva and its churches.

During the proceedings Calvin continued his campaign to bring about a continuance of the trial and utilized the pulpit to his own advantage in condemning heretics in general and Servetus in particular. Calvin also wrote to the various churches under his influence, virtually commanding them to reply in his favor and to ignore any existing precedents dealing with heresy on the pretext that the problem in question was different at this time. In due course of time the churches replied to Calvin. While acknowledging Servetus' guilt regarding certain charges, they refused to recommend the death penalty. However, the verdict from Vienne finally arrived, condemning Servetus and demanding that he be returned to the French authorities. This request went unheeded because the people of Geneva refused to relinquish such a valuable prize who was to afford them the opportunity to display the acme of their particular Christianity; namely, the execution of this heretic.

On Thursday, October 25, 1553, the pronouncement against Servetus

was made public. It was a long tirade of unenlightened convictions and ended in the following words: "Having God and his Holy Scriptures before our eyes, we say in the name of the Father, the Son and the Holy Ghost that this is our final sentence which we give in writing, thou, Michel Servetus, we condemn to be tied and led to Champel and there to be attached to the stake and burned alive with thine book, both written with thine hand and printed, until thine body is reduced to cinders; and thus shall finish thine days in order to give an example to others who might wish to commit similar acts."

During his confinement in prison, Servetus was cruelly treated. Insults were heaped on him, he was poorly fed and was forced to live in filth and discomfort. It was evidently Calvin's desire to cause Servetus the greatest possible degree of humiliation and suffering. Finally, in desperation, Servetus addressed a letter to members of the Council. "He (Calvin) wishes me to decay here; lice eat me alive, my footwear is torn and I have no change of dress. Three weeks ago I demanded to have an audience, but was unable to obtain one. The cold greatly torments me on account of my colics and hernia, which results in other troubles that I am ashamed to write to you about. This is very great cruelty. For the love of God change the condition of affairs, either from pity or duty."

The Council wished to have clothes sent to Servetus but Calvin again interfered and prevented it. Furthermore, the members of the Council wanted a lawyer sent to see Servetus but Calvin again interfered, insisting that this would be utterly useless because the prisoner was already condemned to die and no clemency was possible. The decision of the Council was not unanimous but the few members who dissented lacked the power to force their contentions. An Italian lawyer, Gribaldo, barely avoided serious penalties owing to his efforts on Servetus' behalf. Servetus might have escaped death had he been willing to retract his statements and disavow his beliefs. However, his courage and unswerving faith in his convictions and his implicit belief in the right of self-expression did not permit him to accede to compromising alternatives. Calvin in company with two councilors went to the prison and begged Servetus to repent. Servetus refused. Even Pastor Farel of Neuchâtel visited him and urged him to make retraction, stating that he would not follow him to the stake if he persisted in maintaining his innocence. Farel demanded that Servetus admit his errors and his lies, to which Servetus replied, "I am perhaps mistaken, but I have neither lied nor sinned."

On October 27, shortly after noon a motley procession left the town hall of Geneva. In their midst was Servetus, arms bound, in dirty and tattered clothing, the helpless target of insults and jibes, being led to the site of his execution. The procession comprised the chief magistrate

of the city, other officials; the clergy in their robes and the usual array of curiosity seekers. Pastor Farel walked with Servetus, continuing his plea for repentance. Passing along the Rue St. Antoine and through the gate bearing the same name, the procession wended its way to the location designated for the torture. Finally, mounting the hill, it reached the field of Champel. There, silhouetted against the pastoral landscape, was the ghastly stake with its iron fetters and heaps of faggots. Everything was in readiness for this great exhibition of sixteenth century Christianity.

At the sight of the stake, Servetus fell to the ground in prayer. Again the clergy clamored for a confession of faith but the victim only cried, "Misericordia, misericordia! Jesu, thou Son of the Eternal God, have compassion upon me!" He was then bound to the stake with the iron chains, a crown of green twigs and straw covered with sulfur was placed on his head, and around his waist were tied a volume of his works and a bundle of manuscripts. In this setting, his bearded intellectual face, showing signs of intense suffering, was said to resemble somewhat the Christ, in whose name he died. A shrieking cry pierced the stillness of the scene when the faggots were ignited and the flames spread upward, dashing burning straw and sulfur into his eyes. The faggots were green and burned slowly, and some bystanders threw more inflammable material on the flames to shorten the period of torture. Servetus' last words, uttered in the agony of a terrible death, reiterated his conviction, "Jesu. thou Son of the Eternal God, have mercy upon me!" Could he have said, "Jesu, thou Eternal Son of God!" his life would have been spared.

Thus died, in his forty-fourth year, Michael Servetus, the martyr, a physician, a physiologist, an anatomist and according to the dicta of his contemporaries, a heretic. Ever true to his convictions he died a martyr because of what he believed to be the truth as revealed to him by the Bible.

REFERENCES

Cumston, C. G.: The biography of Michel Servetus, the discoverer of the pulmonary circulation: to which is appended the text of that passage of his work relating to that discovery, followed by an English translation of the same and notes. Boston M. & S. J. 156:451–461 (Apr. 4) 1907.

Osler, William: Michael Servetus. Bull. Johns Hopkins Hosp. 21:1–11 (Jan.) 1910.

ANDREA CESALPINO

(circa 1519-1603)

No doubt exists that Andrea Cesalpino was one of Italy's most outstanding physicians and scientists and that until recent years medical historians have not accorded him the consideration and honor which he justly deserves. Considerable doubt, however, does exist regarding certain important events in his life. For instance, the date and place of his birth have been a controversial issue among historians. The year of his birth has variously been given as 1519, 1524 and 1525. The place of his birth has been declared to be Arezzo (Tuscany) and in Lombardy. Arcieri reveals evidence that Cesalpino was born in Lombardy and brought to Arezzo by his parents when he was a small child.

In Cesalpino's book, "Daemonum investigatio peripatetica," which was printed in Florence in 1580, a letter written by Cesalpino was found attached to the preface. In this letter, addressed to Stephanus Joannes De Tonsis, who was a Milanese patrician, Cesalpino declared himself a countryman of this patrician. Cesalpino was, therefore, evidently brought to Arezzo from Lombardy when a small child.

Considerable historic difference exists regarding Cesalpino's family. His father was said to be John Baptist, a direct descendant of an aristocratic family named Dei Blanci or Dei Bacci. Some historians assert that John Baptist Cesalpino was a distinguished physician and professor of medicine while others contend that he was a mason. Historically, this is beside the point because regardless of his profession or calling he sired a distinguished son. Andrea Cesalpino's paternal grandfather was named Andrea and resided in a small town, named Ochio, in Lombardy. His mother's name was Jane but nothing is known of her family or her

life. Furthermore, no records appear to be available regarding brothers or sisters.

Cesalpino's father, after living in Arezzo for many years, petitioned the authorities for citizenship a few months before Andrea's graduation from medical school. This request was granted on December 16, 1551, and automatically included the entire family. No definite data exist regarding Cesalpino's early childhood but it seems certain that his educational opportunities were not neglected. He studied medicine at the University of Pisa and here secured a well-rounded education under eminent teachers. He studied botany under Luca Ghini, who was the founder and director of the famous Botanical Gardens of Pisa. Under this great teacher's influence Cesalpino acquired an unusual interest in, and knowledge of, this science. Realdo Colombo, the well-known sixteenth century anatomist, was his professor in this field and Vidus Vidius taught him medicine. During Andrea's student days, the study of philosophy was an important part of every university curriculum and this subject was taught by Simone Porzio. Cesalpino's age and year of graduation are also controversial; his age is variously stated as twenty-six, thirty-two, and thirty-six years and one record asserts that he graduated on March 20, 1555, at the age of thirty-six years. However, the previous record of the granting of his father's citizenship was dated December 16, 1551 and in the application, John Baptist Cesalpino had made the statement that his son would graduate in medicine within a few months. This would indicate the year of Cesalpino's graduation as 1552.

Following his graduation no records of his activities are available until 1556 when Ghini, his professor of botany, died and Cesalpino was appointed his successor as director of the Botanical Gardens of Pisa and deputy to the Simplicia Lectures. Cesalpino held these positions for fourteen years. In 1569 he was appointed professor of ordinary practice of medicine at Pisa and he occupied this position until 1591. From 1569 to 1570 he lectured once each week on botany. In 1592 Pope Clement VIII called him to Rome and he was appointed professor of medicine at the Sapienza and also became the Pope's personal physician.

Cesalpino retained these positions until his death, which occurred on March 15, 1603. Death was ascribed to "acute pleurisy" and it may well be that this great physician met his death from pneumonia. He was buried in the church of San Giovanni dei Fiorentini in Rome. Cesalpino had married Gherarda, the daughter of Bernardino Boroncini of Florence. Little is known of her life and family. One son, John Baptist, survived the great physician but it is not known whether other children had predeceased their father. The son, John Baptist, married a girl from a wealthy and noble Roman family but the Cesalpino family apparently ceased to exist at the close of the sixteenth century.

Andrea Cesalpino was of the nobility, probably not through heredity but rather through his achievements and contributions to a nation and civilization which were on the road to cultural ascendancy and willingly honored those who actively and generously participated in this process.

Cesalpino's most important contribution was his discovery and description of the circulation. He was the first to use the term "circulation" (1571). This work antedated Harvey's disquisition by fifty-seven years. Before considering this work in more detail it is desirable to discuss Cesalpino's writings in general because they represented a great diversity of scientific interests and accomplishments. He was admired as a great philosopher and was on occasion designated as "Aristotle reborn." Cesalpino's philosophic concepts centered around the close relationship between the living body, sense, intellect and the outside world (environment).

His first work, "Peripateticarum quaestionum libri V," contained the description of the circulation of the blood together with discussions of a philosophic nature. The book was written in 1569 and first printed at Venice in 1571 and again in 1593. It was dedicated to the Grand Duke of Tuscany, Francis I.

"Daemonum investigatio peripatetica," a work dealing with both medicine and philosophy, appeared in 1580.

In 1583 Cesalpino's third book was printed in Florence. This work, titled "De plantis, libri sedecim," was an extensive botanic treatise wherein he undertook the classification of the vegetable kingdom as known to him and approached the problem from the standpoint of plant structure and function. It was divided into sixteen books and contained carefully mounted and dried specimens.

In 1593, Cesalpino's work on medicine appeared. "Quaestionum medicarum" consisted of two books and among various subjects again asserted and described the circulation of the blood. It was dedicated to the Grand Duke of Tuscany, Ferdinand III.

"De metallicis," a work on mineralogy, was Cesalpino's fifth volume to appear (1596). Here he undertook to classify minerals and hinted at the existence of oxygen in his observation that when lead was in contact with the air, a substance from the air, which became converted into a vapor in damp places, gathered as a rough crust on the lead and increased its weight. He also discussed the origin of fossils and wrote about the crystallization of minerals. This book was dedicated to Pope Clement VIII.

William Harvey (1578–1657) of Folkestone, Kent, has generally been regarded as the discoverer of the circulation. While he contributed generously in expounding the facts by dissection, by astute and intelligent observation and by logical deductions, it is nevertheless important to keep the records of history clear. There is in reality no valid reason

why a discovery should be controversial. Priority of chronology cannot be disregarded and in many great scientific revelations the thought, genius and ingenuity of various workers have participated in the completed work, even though the span of years has separated their efforts. Harvey had the advantage of time and presented his work in its entirety without extraneous subject matter which could well cause the submersion of the central theme. Such was the case of the description of the pulmonary circulation, both by Ibn an-Nafis and Michael Servetus, who, living in different countries and in different ages, submerged their masterpieces in long theologic dissertations. The same influences prevailed to a lesser degree in the case of Andrea Cesalpino.

Historians have tended to ignore Cesalpino's work on the basis that his conclusions were largely the result of fortuitous speculation and that he failed to carry out precise dissections. However, Cesalpino's own words refute these allegations and it is important to present certain evidence to this effect.

Cesalpino dissected animals and followed and determined the course of the flow of the blood. In fact, he was the first to use the word "circulation." He recognized and described the structure and the function of the pulmonary artery and the pulmonary vein and distinguished the differences between them. Furthermore, he described the different origin, course and size of the aorta and the vena cava. Cesalpino contended that the veins could not originate from the liver as believed by Galen and his advocates. The reasons for this conclusion were based on accurate observation, Cesalpino having noted that the vena cava had a greater diameter near the heart than near the liver. This was intelligent reasoning. He also observed the differences in the structure of arteries and veins. Another important observation of Cesalpino was concerned with the continuity of the portal vein with the tributaries of the vena cava within the liver. Previously the belief had existed, as in Galen's teachings, that a gap in these vessels occurred. Cesalpino studied the movements of the beating heart and observed that when the heart contracted dilatation of the arteries occurred and when the heart relaxed in diastole, the arteries contracted. He further dissected the veins to confirm his belief that a functional system of communication between the veins and the arteries existed. Thus, as Cesalpino's observations are analyzed critically, it becomes evident that he was possessed of ample facts permitting him to visualize clearly the circulation of the blood and the function and the relationship of the heart to the general scheme.

The following quotation in translation from Cesalpino's work, "Quaestionum medicarum" (1593), eloquently speaks for itself: "The orifices of the heart are made by nature in such a way that the blood enters the right ventricle of the heart by the vena cava, from which the exit from the heart opens into the lungs. From the lungs there is another

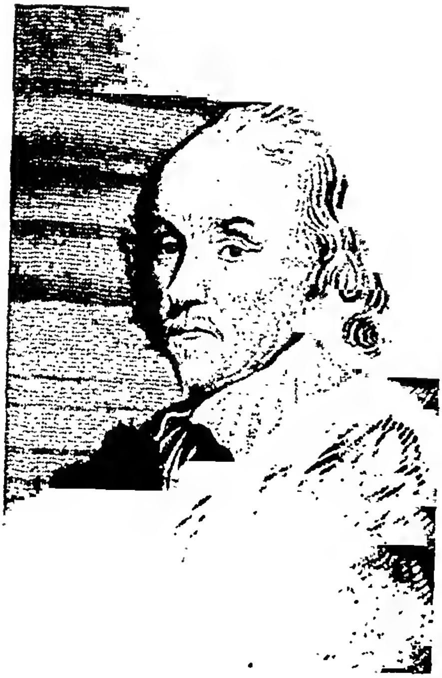
entrance into the left ventricle, from which, in its turn, opens the orifice of the aorta. Certain membranes placed at the openings of the vessels prevent the blood from returning, so that the movement is constant from the vena cava through the heart and through the lungs to the aorta."

REFERENCES

Arcieri, J. P.: The circulation of the blood and Andrea Cesalpino of Arezzo. New York, S. F. Vanni, 1945, 193 pp.

Castiglioni, Arturo: A history of medicine. (Translated by E. B. Krumbhaar.) New York, Alfred A. Knopf, 1941, pp. 436–440.

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, p. 231.



WILLIAM HARVEY

(1578–1657)

No historical medical commentary would be complete without special consideration of William Harvey. He was born in 1578 in Folkestone, Kent, and was the eldest son of Thomas Harvey. His preliminary education was obtained at the Canterbury Grammar School. Following the successful completion of this phase of his training he entered Caius College in Cambridge in 1593. Dr. Caius, the founder and for many years the master of this college, taught Greek and also introduced the study of anatomy into England. Because of Dr. Caius' influence and the high standing of his institution, he was permitted to secure the bodies of two criminals each year for the purposes of dissection and anatomic teaching. No record exists as to Harvey's participation in the dissections, although it is probable that he did interest himself in this study. He graduated from Caius College in 1597 and received the degree of Bachelor of Arts. His collegiate education was undoubtedly comprehensive and included a practical knowledge of Latin and Greek together with instruction in logic, philosophy, mathematics and physics.

Harvey selected Padua for his medical training because this celebrated university was unsurpassed at this time. The prestige of this institution, in a great measure, was attained by the achievements and reputations of two great anatomists. Andreas Vesalius and his successor, Hieronymus Fabricius, were the outstanding anatomists and teachers of their era. Harvey is presumed to have entered Padua in 1598 but no record exists of his entrance there until 1600.

It is of historic interest that the theater in which Fabricius delivered his lectures is still in existence. It contains seats which rise steeply. When

Harvey was at Padua, the theater was new, and the Italian authorities had placed an inscription over the entrance to commemorate the genius and achievements of Fabricius. This great master was without a doubt an inspiration to young Harvey and under his tutelage the student acquired an expert knowledge of anatomy. In his famous work, "De motu cordis," Harvey reverently referred to his former teacher as "the celebrated Hieronymus Fabricius of Aquapendente, a most skillful anatomist, and venerable old man." While Harvey was a student at Padua, Fabricius was carrying out his dissections and investigations concerned with the valves of the veins and the progress of this work and the findings were undoubtedly conveyed to the students. Sylvius of Louvilly (Jacques DuBois, 1478–1555), the teacher of Vesalius at Paris, had described the valves of the veins at an earlier date but this knowledge had apparently been forgotten. Fabricius rediscovered these valves in 1574 but did not correctly conceive their function. Fabricius believed them to be concerned in preventing overdistention of the veins when blood flowed from the larger into the smaller veins and he explained their absence in the arteries on the ground that the blood was in constant motion in a state of ebb and flow. Harvey, however, indicated that the actual function of the valves is to prevent reflux in the veins and that these barriers are important factors in the circulation of the blood.

After four years of study at Padua, Harvey received the degree of Doctor of Physic (1602), which entitled him to practice and teach arts and medicine in every land. Harvey had been a superior student and to attest this fact his diploma bore the following addendum: "He had conducted himself so wonderfully well in the examination, and had shown such skill, memory, and learning that he had far surpassed even the great hopes which his examiners had formed of him."

Harvey returned to England the same year of his graduation and received the degree of Doctor of Medicine from the University of Cambridge. Two years later (1604) Harvey settled in London and married the daughter of a physician (Lancelot Browne, physician to Queen Elizabeth and James I). No children were born to this union. He began the practice of medicine and was elected to fellowship in the College of Physicians in 1607. Two years later he was appointed to the staff of St. Bartholomew's Hospital.

In 1615 Harvey received the honor of appointment as Lumleian lecturer, a position which was sponsored by the College of Physicians. He held this position for the remarkably long period of forty-one years, when he resigned the post. Harvey's first Lumleian lectures were delivered from April 16 to 18, 1616, and covered both anatomic and surgical subjects. The manuscript notes of his first lectures are the property of the British Museum. The second portion of the notes contains a description of the thorax and its contents and here is found his first descrip-

tion of the circulation. These notes are initialed and indicate that Harvey believed his ideas to be original.

> It is plain from the structure of the heart that the blood is passed continuously through the lungs to the aorta as by the two clacks of a water bellows to raise water.
>
> It is shown by the application of a ligature that the passage of the blood is from the arteries into the veins.
>
> Whence it follows that the movement of the blood is constantly in a circle, and is brought about by the beat of the heart. It is a question, therefore, whether this is for the sake of nourishment or rather for the preservation of the blood and the limbs by the communication of the heat, the blood cooled by warming the limbs being in turn warmed by the heart.

It is thus evident that Harvey had definite concepts regarding the circulation as early as 1616, twelve years before the publication of his "De motu cordis."

In 1618 Harvey was appointed physician extraordinary to James I and, on the death of the monarch, his son, Charles I, appointed Harvey a physician-in-ordinary. In addition to his royal duties, Harvey was physician to several prominent families among the nobility. Among his patients was Francis Bacon (1561–1626), whose literary efforts apparently did not impress Harvey, for the latter commented on one of Bacon's books, "He writes philosophy like a Lord Chancellor."

Harvey was a contemporary of Shakespeare and the resemblance between these great personages has been frequently alluded to. It is possible that Harvey was influenced in various ways by his distinguished contemporary.

In 1628 Harvey's monumental work, "Exercitatio anatomica de motu cordis et sanguinis in animalibus," appeared. The original work, written in Latin, was published in Frankfurt am Main. In his first chapter, Harvey indicated that he endeavored to discover the motions and the function of the heart "from actual inspection and not from the writings of others." To achieve this end he resorted to vivisection, ligation and perfusion. He was able to obtain proof of his concept regarding the circulation by the many dissections which he performed on human bodies.

The crux of Harvey's concept was that the actual quantity of blood as determined by measurement made it impossible for the blood to follow any other course than to return to the heart by way of the venous system. This not only gave him definite proof of the circulation of the blood but constituted one of the pioneer investigations utilizing actual measurement in biologic research.

At an early date in his career (1613) Harvey had been elected to the office of censor in the College of Physicians. He was reappointed to this position in 1625 and again in 1629. In 1628 he was appointed treasurer of the same organization and was reappointed the following year. In the same year he received the command of the King to accompany the

Duke of Lennox on his travels on the Continent. He accompanied the Duke until the winter of 1631–1632, when he returned to England. In 1632 he formulated a set of rules for the new library of the College of Physicians. Early in 1633, Harvey was again commanded by the King to journey with royalty, this time to attend Charles I on his trip to Scotland. During this trip he wrote his treatise on "Bass Rock."

In 1634, the legend of the Lancashire witches was a by-word in England. As was the case in the Salem witchcraft episode in New England in 1692, the accusations rested on a child's perjury. Harvey was called on to examine the bodies of some of the arrested "witches" and some of those permitted to live. Owing to his testimony and that of others, four of the seven convicted "witches" were pardoned. Harvey's refusal to be duped by this prevailing nonsense is of importance, because these beliefs were accepted by some physicians as well as by the laity. One of Harvey's colleagues and contemporaries, Sir Thomas Browne (1605–1682), presumably a scientific and tolerant man, affirmed that he believed in witchcraft. Also the great Carl Linnaeus (1707–1778), born more than a century and a quarter after Harvey, asserted in his work, "Nemesis divina," written for his son, that he believed in supernatural punishments.

Another interesting and unique experience befell Harvey in 1635. In this year he was ordered by the King to perform a postmortem examination on the body of Thomas Parr, who is said to have lived to the amazing age of 152 years and nine months. The results of this examination were not published until 1669, when they appeared in Bett's book, "On the source and quality of blood." From the comments contained in this work, Harvey believed that "Old Tom Parr" would have lived even longer had he remained in his native home, Shropshire, and not changed his residence to London and altered his diet by living with a nobleman.

Harvey's close contacts and friendship with the King resulted in his being suspected as a Loyalist. During the early stages of the Civil War in England (1642) a mob of citizen-soldiers entered Harvey's lodgings, stole his possessions and scattered and destroyed his papers. These papers included the records of a large number of dissections, his observations on the development of insects and notes on comparative anatomy.

In 1645 Harvey was elected to the position of warden of Merton College at the University of Oxford. This was the school of which the celebrated John of Gaddesden (circa 1350), one of the earliest Englishmen to write a comprehensive study of medicine (Rosa Anglica, printed in 1492), had been a fellow. As a result of the turmoil resulting from the Cromwellian Civil War, Harvey held this position for only one year.

The surrender of Oxford in 1645 coincides with Harvey's severance from the court and his gradual retirement from public life. This circumstance was due partly to the existing political situation and partly to

his being affected with gout, of which he experienced recurrent attacks. During this time he was writing his treatise, "De generatione animalium," which was published in 1651. In his embryologic studies, Harvey was handicapped by not having a microscope and arrived at an incorrect conclusion regarding fecundation. He believed the fertilization of the ovum to be something incorporeal—"as iron touched by the magnet is endowed with its own powers." Garrison suggested that the true importance of "De generatione animalium" was "that it subverted the ancient concept that life is engendered out of corruption (or putrefaction)."

Also contained in this work is a description of what appears to be the first recorded instance of spontaneous rupture of the left ventricle in the famous case of the young Lord Montgomery.

The College of Physicians was offered a collection of books, a museum of various objects of interest and an assortment of surgical instruments by an anonymous donor. Before the building was completed the identity of the donor was disclosed and the College responded in 1652 by the erection of a statue of Harvey. However, the College still felt under obligation to Harvey and elected him as its president in 1654. He refused this honor owing to his failing health. His attacks of gout were recurrent and he died on June 3, 1657, from a cerebrovascular accident. He was interred in the family vault at Hempstead in Essex.

REFERENCES

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, 996 pp.

Power, D'Arcy: William Harvey. London, T. F. Unwin, 1897, 283 pp.

Smith, Preserved: A history of modern culture. New York, Henry Holt & Company, Inc., 1930, vols. 1 and 2, 1375 pp.

Willis, Robert (translator): The works of William Harvey, M. D. London, The Sydenham Society, 1847, 624 pp.

Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors. St. Louis, C. V. Mosby Company, 1941, pp. 11–17.

MARCELLO MALPIGHI

(1628–1694)

MARCELLO MALPIGHI was born at Crevalcuore, near Bologna, the son of wealthy parents. There appears to be no record of his early life or elementary education. He entered the University of Bologna in 1645 as a student of philosophy but was obliged to interrupt his studies in 1649 because of the sudden deaths of his father, his mother and his paternal grandmother. Because he was the eldest son of the family the burden of the settlement of the estate became his responsibility. There arose numerous controversial issues which made his task very disagreeable. A dispute concerning boundaries between his father's property and the adjoining property of a family named Sbaraglia continued throughout Malpighi's lifetime and remained a constant source of irritation and unrest. The Sbaraglia family not only brought political pressure to bear to obstruct his professional appointments but also privately insulted Malpighi and his wife.

Two years later, in 1651, Malpighi resumed his education and in the meantime had decided to study medicine. One of his professors, Bartolommeo Massari, occasionally invited some of the instructors and students to his home, to disseminate the new work of Harvey and the new concepts of the English philosophers. This little group ultimately formed itself into a club, limited its membership to nine, the number of the Muses, and adopted the name, "Corus anatomicus." Stimulated by Harvey's ideas and particularly by his viewpoint of learning by means of actual observation, they not only met for purposes of discussion but soon were engaged in the dissection of bodies and in animal experimentation. Young Malpighi was soon admitted to membership in

this club and here he acquired basic knowledge which was to enable him later to make his important discovery which has served to perpetuate his name. He was an excellent student and in 1653 achieved his doctorate in medicine and philosophy.

In 1654 Malpighi married Francesca, the sister of his good friend and professor, Massari. There were no children from this marriage. In 1656 Malpighi, who had developed an active medical practice, was appointed to the chair of medicine at the University of Bologna. In the same year, Ferdinand II, Grand Duke of Tuscany, offered him a post in theoretical medicine at the University of Pisa. Malpighi accepted the post and taught at Pisa for three years. There, under the guidance of Duke Ferdinand, a brilliant intellectual activity was stimulated and concerted efforts were made by the entire faculty to broaden the study and investigation of natural knowledge.

It was at Pisa that Malpighi met Giovanni Borelli. Interesting and important events were destined to result from their friendship, which endured for many years. Borelli also had come to the University of Pisa in 1656 at the invitation of Duke Ferdinand as professor of mathematics. Twenty years older than Malpighi, Borelli instructed him in the new mathematics and physics of the school of Galileo. Malpighi in turn interested Borelli in anatomic and biologic matters so that before long the latter was applying his mathematical knowledge in a study of biological phenomena. Borelli's great contribution, "De motu animalium," published after his death (1680 or 1681), revealed the biologic influence of Malpighi. In later years Malpighi became temporarily embittered by certain coarse personal attacks of Borelli but they were later reconciled to each other and they remained intimate friends for many years. As Malpighi evolved new ideas and undertook new researches or whenever he made a new discovery, he always communicated with Borelli, soliciting his opinion.

In 1659, owing again to difficulties involving his late father's estate, Malpighi resigned his position at Pisa and returned to Bologna. There he was reappointed to the chair of medicine, and in 1660 he announced privately to Borelli his discovery of the structure of the lungs. The medium of communication consisted of two letters which were printed in 1661 and constituted Malpighi's first published work.

Malpighi's predecessors, Ibn an-Nafis, Servetus, Cesalpino, and Harvey, had all predicted the existence of a mode of communication between the arteries and the veins but had been unable to demonstrate capillaries as they did not possess adequate means of magnification. (See pages 60, 61, Chapter 4, for historic data on magnification.)

In the two letters which Malpighi sent to Borelli, he described two important discoveries. The first epistle contained his description of the vesicular nature of the lungs and explained the manner in which the

tributaries of the trachea terminate in the alveoli of the lungs. Malpighi was, therefore, the first to demonstrate the anatomic basis for the actual conception of the process of respiration.

The second epistle contained the first actual description of the capillaries. In it Malpighi also demonstrated that the previous predictions of an anatomic communication between the arteries and the veins were correct. The crucial fact on which the concept of the circulation is dependent was thus established. Without the aid of adequate magnification the previous workers who had conceived the circulation of the blood could only predict the existence of this minute intercommunicating vascular network.

Malpighi's experiments were conducted on cold-blooded animals; 112 years later, the Italian Spallanzani (1773) demonstrated the capillary circulation in warm-blooded animals.

In 1665, in a treatise, "De omento pinguedine, et adiposis ductibus," Malpighi demonstrated the red blood corpuscles. Under his microscope he observed flat red cells in the mesenteric blood vessels of the hedgehog. Apparently, he mistook the red corpuscles for globules of fat passing into the current of blood. This misinterpreted observation was later clarified by van Leeuwenhoek who, in 1674 in the Philosophical Transactions of the Royal Society, gave the first accurate description of the red corpuscles.

In addition to discovering the capillary circulation and being the first to observe the red blood corpuscles, Malpighi worked on the structure of the glands and glandular organs. He is also regarded as the founder of descriptive embryology, because of his researches on the chick embryo, although earlier workers had been interested in the same problem. He also discovered the "rete mucosum" or the Malpighian layer of the skin and further proved that the papillae of the tongue contain the organs of taste.

In his monumental work on the structure of the viscera, "De viscerum structura, exercitatio anatomica," published at Bonn in 1666, Malpighi contributed to the knowledge relating to the physiology of the liver, spleen and kidneys. Also in this work is the first account of the generalized enlargement of the lymphatic nodes with nodules in the spleen. more completely described and defined by Thomas Hodgkin in 1832. During his later years, Malpighi spent much of his time in researches on the anatomy of the silkworm and the morphology of plants. In 1684 his home in Bologna was destroyed by fire, his microscopes were lost and many of his important manuscripts and notes were consumed by the flames.

In 1691, the new Pope, Innocent XII, invited Malpighi to come to Rome in the capacity of his personal physician. Malpighi at first refused but later accepted at the insistence of the Pontiff, who was an old friend.

Soon after his arrival in Rome Malpighi became ill. In July, 1694, he had a mild apoplectic attack and on November 28 a second attack took place. His death occurred on the following day.

REFERENCES

Foster, Michael: Lectures on the history of physiology during the sixteenth, seventeenth and eighteenth centuries. Cambridge, University Press, 1901, 310 pp.

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, pp. 255–256.

Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors. St. Louis, C. V. Mosby Company, 1941, pp. 87–91.

JOHN BAPTIST MORGAGNI

(1682–1771)

MORGAGNI WAS BORN on February 25, 1682, at Forli, near Bologna. His intellectual potentialities were apparent at an early age. At the age of fourteen years he had already written essays and poetry and had publicly discussed philosophic subjects. In 1698, at the age of sixteen years, Morgagni entered the University of Bologna. Here he studied anatomy under the celebrated Valsalva, from whom he acquired his interest in pathology which ultimately was to become his life's work. He was graduated from Bologna in 1701 with high honors in both medicine and philosophy.

Soon after graduation Morgagni accepted the position of prosector in anatomy at Bologna under his professor Valsalva. Valsalva had been a student of the famous Malpighi, discoverer of the capillary circulation. Morgagni aided Valsalva in the preparation of the latter's work on the anatomy and diseases of the ear, "De aure humana," published in 1704. In 1706, Morgagni was elected president of the Academia Inquietorum. In the same year he published his first medical work, "Adversaria anatomica prima," comprising the essence of his discussion before the Academy. In this work were the results of his discoveries concerning the muscles of the hyoid bone, the uvula and the larynx.

Morgagni resigned his position at Bologna and temporarily renewed his study of anatomy at Padua and Venice. After two or three years of graduate study he returned to his home in Forlì to practice medicine. Morgagni was a successful practitioner but the routine duties of practice did not appeal to him, and, therefore, on the death of Domenico Guglielmini, he accepted the chair of theoretical medicine at the University of

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Padua, made vacant when Antonio Vallisnieri succeeded to Guglielmini's post.

In 1715 Morgagni became professor of anatomy at Padua. He was one of a long line of distinguished teachers to hold this position, including Vesalius, Fallopius, Gasserius and Spigelius. This vacancy was created by the death of Michel Angelo Molinetti. During his tenure at Padua Morgagni published his second work, "Adversaria anatomica altera," which dealt chiefly with adipose tissue, the musculature of the gastro-intestinal tract and the structure of the lungs and biliary tract. In this post, Morgagni inaugurated his long and productive career, for he taught at Padua until his death, fifty-six years later.

Shortly after coming to Padua, Morgagni married a lady of the nobility, Paola Vergieri, of Forlì. Fifteen children were born to them, eight of whom were living when Morgagni died.

Morgagni was highly esteemed by his students and his distinguished friends, who according to Pettigrew, included King Charles Emmanuel I of Sardinia and Popes Clement XI, XII and XIII and Benedict XIV. In his own profession, he enjoyed an international reputation and was esteemed by such famous men as Valsalva, Albertini, Lancisi, Verheyen, Heister, Ruysch, Boerhaave, Mead, Sénac, Haller, Meckel, LeClerc, Fantoni, Nigrisoli, Michelotti, Molinetti and many others.

Morgagni received scientific honors from all Europe. He was elected a member of the Academia Naturae Curiosorum in 1708, the Royal Society of London in 1724, the Academy of Sciences of Paris in 1731, the Imperial Academy of St. Petersburg in 1735 and the Academy of Berlin in 1754.

Apart from his scientific studies, Morgagni was a man of many accomplishments. He wrote on philosophy, archaeology, literature and history. Nicholls mentioned these works as typical: Morgagni's letters to Lancisi on the "Manner of Cleopatra's death," "Commentaries" on Celsus and Sammonicus, and notes on Varro, Alpinus, Vegetius, Columella and Vitruvius, as well as archaeologic papers on the districts around Ravenna and Forlì.

It was not until 1761, when Morgagni was seventy-nine years old, that his monumental work, "De sedibus et causis morborum per anatomen indagatis libri quinque," was published. This work has immortalized Morgagni as the father of pathologic anatomy, largely because the records of postmortem examinations are correlated with clinical observations. Furthermore, he was the first to describe many diseases. Prior to Morgagni's work, the standard printed work on pathologic anatomy was the "Sepulchretum" of Theophilus Bonetus, published at Geneva three years before Morgagni was born. The more Morgagni studied the "Sepulchretum" the less satisfied with it he became. Therefore he concluded to supplement it with his own observations and experiences.

As was the custom of the time, Morgagni wrote his observations in the form of letters or epistles to a friend, a procedure that eventuated in the production of seventy letters. The letters were later returned to Morgagni and were revised and published in a huge work of five books.

The five books of "De sedibus et causis morborum" dealt with: (1) diseases of the head, (2) diseases of the thorax, (3) diseases of the abdomen, (4) diseases of a general nature and diseases requiring surgical treatment, and (5) miscellaneous conditions. The work was based on the findings in 640 postmortem examinations chiefly occurring in his own experience but occasionally extracted from the unpublished notes of Valsalva and Albertini.

Morgagni devoted several letters in this work to a study of the diseased heart. In these letters he accurately described the principal cardiac lesions which he observed at postmortem examinations. Among them were descriptions of mitral stenosis, heart block, calcareous stenosis of the aortic valve with regurgitation, coronary sclerosis and aneurysm of the aorta. Also contained in this collection was a description of angina pectoris which he had recorded in 1707. Morgagni observed that certain disorders, such as asthma and dyspnea, previously ascribed to pulmonary disease, also might be caused by diseases of the heart. Like many of his predecessors, he suggested the possible relationship of syphilis to aneurysm. He described rupture of the heart but did not mention its cause. He also described vegetative endocarditis.

Nicholls emphasized the fact that Morgagni "came far short of establishing a complete system of Morbid Anatomy." Morgagni could not entirely rid himself of the erroneous concepts of disease prevalent in his day. Although the microscope was in use before his time, he does not appear to have used it in his researches. Nevertheless, by basing his views on personal observation and making an effort to correlate clinical phenomena of disease with morbid changes, Morgagni established a sound basis for those cardinal principles that underlie modern methods of scientific investigation.

Morgagni continued to teach to the last year of his life and delivered lectures in spite of the rigors of an excessively cold and severe winter. In 1764 John Morgan, of Philadelphia, visited Morgagni at Padua and later recorded the statement that the old gentleman was as hale and hearty as a man of fifty years and continued to carry on his activities without the aid of spectacles. Morgagni presented Morgan with a copy of "De sedibus" which is now in the College of Physicians of Philadelphia. According to Castiglioni, an erroneous legend resulted from this gift in which it was rumored that the donor had inscribed himself as a cousin. This was probably suggested by the similarity of the names, Morgagni and Morgan.

In 1769 the Natio Germanica of the Paduan Athenaeum publicly

honored Morgagni in the magnificent aula of the university. In Italy, admirers often referred to him as "His Anatomical Majesty."

Morgagni's death occurred on December 5, 1771, in his ninetieth year. It is of interest to note that the cause of death was spontaneous rupture of the heart, which according to modern knowledge is usually the result of acute myocardial infarction. The citizens of Forlì, the town of his birth, erected a bust to Morgagni in 1763 and placed it in the principal palace of the city. More than a century and a half after his death, in 1931, the people of Forlì again honored their distinguished son by erecting and unveiling a monument in the piazza inscribed with his name. At the same time a commemorative volume was published which was composed of a voluminous collection of Morgagniana.

REFERENCES

Adams, E. W.: Founders of modern medicine: II. Giovanni Battista Morgagni (A. D. 1682–1771). M. Libr. & Hist. J. 1:270–277, 1903.

Castiglioni, Arturo: A history of medicine. (Translated by E. B. Krumbhaar.) New York, Alfred A. Knopf, 1941, 1013 pp.

Long, E. R.: A history of pathology. Baltimore, Williams & Wilkins Company, 1928, 291 pp.

Nicholls, A. G.: Morgagni, the father of modern pathology; an appreciation and a comparison. Montreal M. J. 32:40–51 (Jan.) 1903.

Pettigrew, T. J.: John Baptist Morgagni, M.D., F.R.S. In: Medical portrait gallery. Biographical memoirs of the most celebrated physicians, surgeons, etc. etc., who have contributed to the advancement of medical science. London, Fisher, Son & Co., 1840, vol. 1, p. 10.

Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors. St. Louis, C. V. Mosby Company, 1941, pp. 171–175.

JOSEPH LEOPOLD AUENBRUGGER

(1722–1809)

JOSEPH LEOPOLD AUENBRUGGER, the son of an innkeeper, was born at Graz, in Styria, Austria. Not much is known of Auenbrugger's childhood or early education except for the fact that he was musical and undoubtedly received instruction in music. Before he was sixty years old, Auenbrugger wrote the libretto for Antonio Salieri's "Der Rauchfangkehrer, oder die unentbehrlichen Verrater ihrer Herrschaften aus Eigennutz." This musical composition was presented at Vienna in 1781 and attracted the favorable notice of the Empress Maria Theresa, who requested him to write another. He declined with the comment that he had more important tasks to perform. This was not an irrelevant incident, for no doubt exists that Auenbrugger's musical ear and his fine perception of sound played an important part in his great discovery.

Auenbrugger studied medicine at the University of Vienna and was a student under van Swieten, who in turn had been a pupil of the celebrated Boerhaave at Leyden. Van Swieten had come to Austria from Holland at the request of the Empress Maria Theresa, became court physician and through his support by the royal house was able to establish the great medical school in Vienna.

During his student days, Auenbrugger met Marianna von Priestersberg and the couple were married in 1754. Two daughters were born to this union; one became an accomplished pianist, while the other was noted for her beauty and wit.

From 1751 to 1762 Auenbrugger was associated with the Spanish Hospital at Vienna, first as assistant and later as physician. Here he began his studies which later culminated in his great discovery. Two im-

portant facts must be recalled at this point of the narrative. The first, already mentioned, has to do with his musical talents and keen perception of sound. The second relates to his boyhood and the occupation of his father. In those days the process of tapping was used to determine whether walls were solid or contained hollow hiding places and innkeepers employed the method to determine the fluid level of the contents of kegs. Remembering these duties of his boyhood, Auenbrugger could well have conceived the idea of utilizing the same method in the examination of the human thorax.

In 1754 he first noted the difference in sounds produced by striking the wall of the thorax in various places. Only after seven years of untiring and diligent investigation did Auenbrugger record and publish his observations. His book "Inventum novum ex percussione thoracis humani ut signo abstrusos interni pectoris morbos detegendi," was published in Vienna in 1761.

After describing the sound produced by striking the thorax of a healthy person in different regions, Auenbrugger presented a detailed account of his method of performing percussion. It is possible that if he had applied his ear as well as his hand he might have anticipated Laënnec. Nevertheless he came near to the discovery of auscultation when he stated under part three of his Eleventh Observation in "On percussion of the chest": "If at this time, while the patient is coughing and spitting, the palm of the hand be placed over the site of the vomica, i.e. over the place where its existence had been detected by percussion—the noise of fluid within the chest will be sufficiently manifest."

It is important to note, especially, the diseases which he was able to detect solely by means of the abnormal sounds elicited by percussion, diseases that he was later able to confirm by postmortem examination. According to Auenbrugger these detectable diseases included "scirrhus" of the lungs, vomica, empyema, pleural effusion, pericardial effusion, extravasation of blood into the cavity of the pleura or pericardium and aneurysm of the heart (dilatation of the heart).

Auenbrugger's discovery was quite generally ignored even by the outstanding physicians of his time. Even his own teacher, van Swieten, for whom Auenbrugger had the greatest regard, was not impressed by this remarkable new aid to diagnosis. The only prominent physicians who appreciated Auenbrugger's work at that time were Dr. Stoll of Vienna, who both employed and taught percussion from 1776 to 1784, and Charles G. Ludwig of Leipzig. The "Inventum novum" was translated into French by Rozière of Montpellier in 1770. Although the book went through two French editions it seems to have been practically unknown until the great clinician Jean-Nicolas Corvisart, noted teacher of Laënnec and physician to Napoleon Bonaparte, revived and emphasized the importance of the discovery.

It is said that Corvisart had never heard of Auenbrugger's work until he read of it in the works of Stoll. From that time on he practiced percussion with perseveranee on living subjects as well as on cadavers. After twenty years of experience with pereussion he translated Auenbrugger's original book and added his own voluminous eommentaries to it in 1808, only a year before Auenbrugger's death. Corvisart, in his 440-page translation, gave full credit to Auenbrugger as the discoverer of pereussion but it was Corvisart's renown at home and abroad that rapidly placed the diseovery of Auenbrugger in an exalted position. In Corvisart's preface, according to Otis, he stated: "I declare from experienee, that this sign of which I treat is one of the greatest importanee, not only in detecting disease, but also in curing it, and therefore merits first place after exploration of the pulse and respiration."

Even though Auenbrugger's new method of physieal diagnosis was not accepted during his lifetime, he nevertheless enjoyed respect as a physician and developed a large praetice. He was noted for his philanthropies and his services were graciously rendered to the poor as well as to the wealthy.

As previously mentioned, Auenbrugger had found favor with the Empress Maria Theresa early in his professional career. The Emperor Joseph ennobled him in 1784, not because of his discovery but rather in recognition of his skill as a physieian and his services to the public and the poor.

In the latter part of his life Auenbrugger lost the sight of one eye but the sight in the other eye was so perfect that he eould tell time by the town clock, which was a considerable distance from his window. Auenbrugger's wife predeceased him by two years. (In 1804 they had celebrated their golden wedding anniversary.) Following this bereavement, Auenbrugger took little interest in life, spent most of his time in his library and enjoyed only the company of his granddaughters. His death, the result of an acute respiratory infeetion, occurred in his eighty-seventh year.

REFERENCES

Nova et vetera: Leopold Auenbrugger; the discovery of percussion. Brit. M. J. 1:1191–1192, 1909.

Otis, E. O.: Auenbrugger and Laennec, the discoverers of percussion and auscultation. Boston M. & S. J. 139:281–285; 305–308, 1898.

Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors St. Louis, C. V. Mosby Company, 1941, pp. 189–213.

WILLIAM WITHERING

(1741-1799)

WILLIAM WITHERING combined his talents in order to bestow on mankind a gift of inestimable and enduring value. He was by choice a physician, respected in his community as an able practitioner and acknowledged by his friends and colleagues as a humble and capable scientist. In addition to these qualities, he was possessed of a broad knowledge of botany which contributed in a great measure to the creation of his outstanding work.

Withering was born on March 28, 1741 at Wellington, Shropshire, in the Midlands of England. His father, Edmund Withering, was an apothecary and a practicing physician and a highly respected citizen of his community. Withering's maternal uncle was a physician in Lichfield and his maternal grandfather, Dr. George Hector, was also a physician and the one who attended the birth of the famous Samuel Johnson. With this professional heredity there is little wonder that young Withering was attracted to the study of medicine.

Withering, according to the custom of the times, received his early instruction through private tutorship. This task was assigned to the Reverend Henry Wood of Ercall, who instructed the boy in the elements of the classics, mathematics, geography and history. In 1762 Withering entered the University of Edinburgh, where he studied medicine and other sciences. Among the required sciences of the curriculum was botany. While engaged in these studies the young student asserted in a letter to his parents that botany was distinctly disagreeable to him. It is of unusual interest that this distaste for botany was later converted into a pleasurable and scientifically profitable avocation

Among Withering's professors were Hope in botany, Whytt (an authority on hysteria) in medicine, Alexander Monro "Secundus" (who in 1769 described the foramen of Monro) in anatomy and Cullen in chemistry and medicine. Withering had high regard for William Cullen (1712–1790), who held chairs of medicine and chemistry at both Edinburgh and Glasgow. Cullen was one of the first professors in Great Britain to present clinical lectures. These lectures established a precedent in that they were delivered in English instead of the customary Latin. Withering received the degree of Doctor of Physic in 1766; his thesis was "De angina gangraenosa" (malignant sore throat). Even before his graduation, Withering delivered several short talks on rachitis and dropsy before the Medical Association of Edinburgh. In addition to his interest in medicine he also maintained an interest in literature and music and learned to play the bagpipes and the flute.

Before establishing himself in the practice of medicine Withering decided to spend some time in traveling; therefore in company with a friend he set sail for France. While on this trip Withering's friend died, presumably of tuberculosis. The journey was abruptly interrupted and Withering was compelled to return to England. He spent the ensuing winter at his home, assisting his father in medical practice. During this time he sought a location that offered opportunities for a young practitioner. In the meantime, the physician in the nearby town of Stafford had died and Withering concluded to establish his practice there. He remained in Stafford from 1767 to 1775. As his practice was not too time consuming, he utilized much of his leisure in studying the local flora and perfecting his knowledge of botany. During this period Withering accumulated extensive notes which formed the basis of his first book, "A botanical arrangement of all the vegetables naturally growing in Great Britain." This work, published in London in 1776, appeared in several editions. It included accurate descriptions of the plants together with their uses. While still in Stafford, Withering became acquainted with a young lady of artistic tendencies who was particularly interested in painting flowers. She was also his patient. During his botanical forays he furnished Helena Cook with suitable flowers to paint. Their friendship eventuated in love and they were married in 1772.

In 1775 Withering decided to leave Stafford and to seek the greater professional opportunities afforded by a larger community. His friend, Dr. Erasmus Darwin, grandfather of the celebrated Charles Darwin, urged him to establish practice in Birmingham. In this new environment, Withering met many interesting people and soon became a member of the Lunar Society, a group of congenial scientists whose membership included truly historic personages. Among them were Dr. Erasmus Darwin, James Watt, the inventor of the steam engine, Joseph Priestley, the English discoverer of oxygen, and a prominent industrialist named

Boulton. Many famous visitors attended meetings of the Society, including such celebrities as Solander of Sweden, Linnaeus' student, and Benjamin Franklin.

Withering's practice grew rapidly and soon was reputed to be the best outside of London. He aided in the completion of the general hospital at Birmingham and in his own home gave free medical counsel to the poor on certain days each week. Withering's extensive practice frequently caused him to travel both day and night. The loss of time thus incurred prompted him to have a lamp installed in his carriage so that he was able to read and write during night journeys. During time spent in this manner he wrote his article, "An account of the scarlet fever and sore throat, or scarlatina anginosa" (London, 1779). In addition to the practice of medicine and his explorations in the realm of botany, Withering interested himself in mineralogy and chemistry. In 1783 he translated a work by Bergman on mineralogy. Werner, the German geologist, honored Withering following the latter's discovery of natural barium carbonate (terra ponderosa) by naming the mineral "witherite." In 1784 the Royal Society elected Withering a fellow and in 1791 the Linnaean Society bestowed similar recognition. He shunned other affiliations because the bulk of his time and resources was devoted to his work.

At this time, Withering was at the height of his career and many distinguished visitors from the Continent came to Birmingham to interview him. The eminent French botanist, L'Héritier de Brutelle, named a plant Witheringia solanacea in his honor.

As early as 1776 Withering's health began to fail and he observed the first symptoms of his pulmonary tuberculosis. For several preceding winters he had suffered from acute upper respiratory infections and in the winters of 1783 and 1784 he was forced to cease practice for considerable periods.

In 1785, Withering published his little book, "An account of the foxglove," which remains today one of the brilliant classics of medical literature. In this work on the foxglove Withering stated that his attention had been drawn to the plant in 1775 by the discovery that it was important in the treatment of dropsy. A remedy used by an old woman in Shropshire, "Old Mother Hutton," had been effective in relieving dropsy when the therapeutic efforts of reputable physicians had failed. After carefully analyzing this remedy, which was a decoction of herbs and leaves, Withering found that the active and important ingredient was foxglove (digitalis). After experimenting with foxglove at great length and carefully observing its effects he finally administered it to his patients in his private dispensary. His interest in the drug became heightened when he learned that the principal of Brasenose College, Oxford, had received great benefit from its administration. Withering

first made a decoction from the leaves of the foxglove but later prepared an infusion and at times used the leaves in the form of a powder. The news regarding the value of digitalis in the treatment of dropsy spread rapidly among Withering's friends and associates both in Birmingham and in Edinburgh. In 1783 the drug appeared in the Edinburgh Pharmacopoeia for the first time.

It would be of great importance for every practicing physician to read Withering's book because many errors of administration of digitalis which prevail today might be avoided. He recommended the drug in cases of dropsy and anasarca only and carefully analyzed conditions in which it was not beneficial. His book was a curb on the indiscriminate use of digitalis which, then as now, occurred as its administration became more widespread. Withering did not clearly understand the action of digitalis in dropsy nor did he differentiate its action on cardiac dropsy from its effects on other forms of dropsy. However, he was aware that it exerted some action on the heart and that it caused slowing of the pulse, for he stated "that it has a power over the motion of the heart, to a degree yet unobserved in any other medicine, and that this power may be converted to salutary ends."

In 1786, because of the state of his health, Withering felt compelled to move to the country. He chose Edgbaston Hall, which then was well beyond the limits of Birmingham but not too far distant to permit him to carry on his practice. In addition to managing his estate he was able to spend considerable time out of doors and became particularly interested in breeding Newfoundland dogs. He also had two pet monkeys and, when one of them became ill with fever, cough and emaciation and finally died, he recorded the postmortem findings as "phthisis pulmonalis similar to that found in human victims." When Withering recorded this comment he probably thought of the fate that awaited him.

In 1790, Withering became severely ill and began to experience severe dyspnea and marked exhaustion. However, he continued to carry on his practice in a limited manner and pursued his other interests to the capacity of his strength and reserve. The limitations of his efforts caused him to state: "The languor of illness is one of the most mortifying symptoms to those who dislike indolence." The unsettled political conditions of England influenced Withering, for he was not able either to maintain peace of mind or to obtain the physical relaxation so necessary for a victim of tuberculosis. He was a moderate progressive and held the conviction that the constitution under King George III required modifications. In spite of his rather passive political views and probably because he was sympathetic to the French revolutionists, Withering's home was ransacked and he was forced to leave when the home of Priestley was burned in 1791 by a mob. He succeeded, however, in

saving his library and his collection of scientific items by concealing and moving them in wagons loaded with hay.

Withering had retired from the active practice of medicine in 1783 because of his progressive decline in health. He spent the winter of 1792 in Portugal to escape the climatic rigors of the British Isles. At Lisbon he continued his botanical researches and also made an analysis of the waters of the springs at Caldas da Rainha. Withering felt that his health had not been benefited by his stay in Portugal, although he again spent the following winter in this warm climate.

After his return to England, Withering spent much of his time in his library but was harassed by cough, shortness of breath and exhaustion. At times he was so exhausted that he experienced difficulty sitting at his desk. Concluding that the exposed location of Edgbaston Hall no longer was suitable to his failing health, he decided to change his living quarters. Withering acquired Priestley's home, which had been partly destroyed by a mob in 1791, and ordered it rehabilitated. His new home, "The Larches," proved to be a disappointment, for only eight days after he moved in, death claimed him, on October 6, 1799.

Withering was buried in the old church at Edgbaston. In this church is a tablet of black marble inscribed with his name and the emblem of Aesculapius surrounded by flowering digitalis and Witheringia solanacea.

REFERENCES

Cushny, A. R.: William Withering, M.D., F.R.S. Proc. Roy. Soc. Med. (Section of the History of Medicine.) 8:85–94 (Mar. 17) 1915.

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, pp. 356–357.

Kolipinski, Louis: William Withering and his book on the foxglove. M. Rec. 86:8–14, 1914.

Nylin, Gustav: William Withering—a bicentenary tribute. Am. Heart J. 25:285–297 (Mar.) 1943.

Roddis, L. H.: William Withering and the introduction of digitalis into medical practice. Ann. M. Hist. n.s. 8:93–112; 185–201, 1936.

Shryock, R. H.: The development of modern medicine: an interpretation of the social and scientific factors involved. Philadelphia, University of Pennsylvania Press, 1936, pp. 1 and 2.

Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors. St. Louis, C. V. Mosby Company, 1941, pp. 225–230.

RENÉ-THÉOPHILE-HYACINTHE LAËNNEC

(1781-1826)

THE MAN WHOSE discovery was destined to revolutionize the diagnosis of diseases of the heart and who proved to be the vital force that enabled this branch of medicine to forge ahead with unprecedented vigor, was René-Théophile-Hyacinthe Laënnec. He was born at Quimper in Lower Brittany, on February 17, 1781, the first child of a sickly mother. René was a frail child and even in adult life remained thin and appeared undernourished.

Laënnec's father was a lawyer and apparently not very successful, as indicated by his inability to assume the responsibility of his family. Another son, Michel, was born a year after René. A daughter, Marie, was born three years later; another daughter was born in 1786 but lived only a few days. Soon thereafter the mother died and the two little boys were sent to live with their paternal uncle, Michel, the rector of a parish in Elliant. The children remained with the rector for a year. When he left for England they were placed in the care of another uncle, Guillaume-François Laënnec. He was a famous physician, a former pupil of the celebrated John Hunter, and at this time was Professor of Medicine at Nantes. He was a learned scholar, not only proficient in medicine but also interested in the humanities, the Greek classics, and was an able writer and lecturer. This famous uncle inspired René not only to acquire a well-rounded preliminary education but later to choose medicine as his career.

The two brothers attended L'Institution Tardivel for three years. In 1791 René entered the Collège de l'Oratoire where he studied re-

ligion, political science, orthography, grammar, geography, Latin prose and poetry.

During these formative years, young René, like countless other French children, was subjected to the horrors of the French Revolution. Near his home in Nantes a guillotine was within sight of the square and he witnessed several executions. His uncle Guillaume was imprisoned for six weeks on suspicion of being out of sympathy with the contemporary government. The Revolutionaries, Mirabeau, Danton, Robespierre, Marat and Carnot, were in power and were in the process of reshaping the destinies of millions.

Medicine found itself in a chaotic state during the critical years around 1789, partly from the direct effect of the revolution and partly from disharmony among the medical profession itself. Many prominent physicians became members of the revolutionary assemblies. Among these were Jean-Gabriel Gallot (1743–1794); Joseph-Ignace Guillotin (1738–1814), the inventor of the penal decapitating device which is still known by his name; François-Pierre Blinn (1758?–1834); Jean-Louis Frison-Jaubert (born about 1756) and others. The number of medical students decreased so rapidly that hardly more than six or seven graduated at Paris each year and between 1786 and 1789 not a single student was graduated by the Paris Faculty. It was toward the close of this chaotic period that Laënnec undertook the study of medicine.

In 1793 he entered the National Institute and two years later, at the age of fourteen and a half years, he began the study of medicine. It was at L'Hôtel Dieu at Nantes that Laënnec began his medical studies. One quarter of the 400 beds were in charge of his uncle, Guillaume-François Laënnec, and at the time these were largely occupied by sailors afflicted with tropical diseases. In addition to studying medicine, young Laënnec found time to apply himself to the study of botany and Greek.

Laënnec completed his studies at Nantes in five years and was then sent to Paris, where he entered L'École de Médecine and became a student of the famous Corvisart. He had great admiration for his teacher and Corvisart inspired the young man and interested him particularly in diseases of the heart and lungs. During his student days, Laënnec collected Corvisart's aphorisms which he later published. Other teachers of Laënnec were Marie-François-Xavier Bichat (1771–1802) in physiology and medicine and Baron Guillaume Dupuytren (1778–1835), the celebrated French surgeon.

Laënnec's first published work occurred while he was still a student. In 1802 he described the findings observed at postmortem examination on a patient who had died from heart disease. The mitral valve was found to be "ossified" and the left ventricle dilated. This was un-

doubtedly an instance of mitral stenosis. In March, 1804, shortly before his graduation, Laënnec delivered a lecture wherein he established the fact that phthisis is tuberculosis of the lungs. From then on the disease became known as pulmonary tuberculosis. He received his doctor's degree in June of the same year. His graduation thesis was entitled "Propositions on the doctrines of Hippocrates in regard to the practice of medicine" (translation).

During the ensuing five years Laënnec lectured on pathologic anatomy, conducted a small private practice and contributed articles to medical journals, medical dictionaries and encyclopedias. Some of his articles were published in the Journal de Médecine, of which he was an editor from 1805 to 1808. During his editorship, Laënnec, who was bitterly opposed to the fantastic tenets of his countryman and contemporary, François-J.-V. Broussais (1772–1838), expressed himself in editorials and articles. Broussais fostered the strange belief, which he named "physiologic medicine," that disorders of function were all-important to the exclusion of changes of structure, and that disease depended on local irritation, especially of heat, which controlled the chemical processes of the body. In his concept of pathology, Broussais believed that all diseases centered around the existence of gastro-enteritis. He denied the premise that nature is endowed with any healing powers and believed that it is necessary to prevent disease by active measures. Broussais was an unusually enthusiastic bloodletter and used leeches prodigiously. According to Garrison, 41,500,000 leeches were imported into France in 1833.

Laënnec's early works included a description of the pathology of peritonitis (1803), a description of the capsule of the liver (1803), the first accurate description of melanosis (1806) and the description of an extraperitoneal hernia (1812). He became physician to the Beaujon Hospital, where he became especially interested in diseases of the thorax and employed the method of percussion, learned from his teacher, Corvisart. It was Corvisart who established Auenbrugger's discovery of 1761 in medical practice.

In 1816, Laënnec was appointed to the staff of the Necker Hospital and while there, in 1819, discovered the method of auscultation. His publication, "Traité de l'auscultation médiate" (1819), is one of the prized classics of medical literature. In this remarkable work, Laënnec not only described the wooden cylinder (the first monaural stethoscope) but also detailed the normal and abnormal sounds revealed by this new method of diagnosis as well as the interpretation of these sounds in the identification of diseases of the heart and lungs. In his directions for the making of the cylinder, he recorded the interesting note (in translation), "Any turner will be able to make the instrument from the above description."

In the following excerpt from the introduction to the second part of his famous book, Laënnec interestingly relates the circumstances leading to his discovery of auscultation.

In 1816, I was consulted by a young woman labouring under general symptoms of diseased heart, and in whose case percussion and the application of the hand were of little avail on account of the great degree of fatness. The other method just mentioned being rendered inadmissible by the age and sex of the patient, I happened to recollect a simple and well-known fact in acoustics, and fancied at the same time, that it might be turned to some use on the present occasion. The fact I allude to is the augmented impression of sound when conveyed through certain solid bodies, as when we hear the scratch of a pin at one end of a piece of wood, in applying our ear to the other. Immediately, on this suggestion, I rolled a quire of paper into a sort of cylinder and applied one end of it to the region of the heart and the other to my ear, and was not a little surprised and pleased, to find that I could thereby perceive the action of the heart in a manner much more clear and distinct that I had ever been able to do by the immediate application of the ear. From this moment I imagined that the circumstance might furnish means of enabling us to ascertain the character, not only of the action of the heart, but of every species of sound produced by motion of all the thoracic viscera.

The physicians of France received Laënnec's discovery of auscultation with indifference and skepticism, but those of foreign countries, especially those of the British Isles, not only acclaimed the discovery but sought personal instruction at his clinic in the Necker Hospital. In 1822 Laënnec was appointed professor of medicine at the Collège de France and at the same time was elected to membership in the Académie de Médecine of France. A year later, he succeeded his eminent teacher, Corvisart, in the Collège and in 1824 the knighthood of the Legion of Honor was conferred on him.

In the same year Laënnec married his housekeeper, Madame Argou, a sickly woman who was a year older than he. This marriage, it was said, was one of convenience and not of love, for Laënnec was in poor health and needed care. For several years he had been a sufferer from asthma and following an acute respiratory infection he became seriously ill and died at the age of forty-five years on August 13, 1826.

In 1867 the Boston Medical and Surgical Journal called attention to the fact that 20,000 francs had been collected during that year to erect a monument to Laënnec, the money having been raised chiefly in France but in part by the Medico-Chirurgical Society of London and also by physicians in Scotland, Ireland, Prussia and Austria. Modeled by Lequesne and cast by Ducel, the monument was exhibited at the Paris Exposition and was dedicated in May of 1868.

REFERENCES

Chevalier, A. G.: Medicine and the natural sciences in France during the Napoleonic era. *Ciba Symp.* 3:964–969 (Sept.) 1941.

Chevalier, A. G.: The physicians in the revolutionary assemblies. *Ciba Symp.* 7:239–249 (Feb.) 1946.

Garrison, F. H.: Laennec. (Editorial.) Bull. New York Acad. Med. s. 2, 2:389–393, 1926.

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, pp. 411–413.

Medical Intelligence (news note): Monument to Laennec. Boston M. & S. J. 76: 382, 1867.

Robinson, Victor: René Théophile Hyacinthe Laennec (1781–1826) M. Life. 28: 456–469, 1921.

Webb, G. B.: René Théophile Hyacinthe Laënnec; a memoir. New York, Paul B. Hoeber, Inc., 1928, 146 pp.

JOSEPH SKODA

(1805–1881)

JOSEPH SKODA WAS born, the son of a locksmith, at Pilsen, in Bohemia, in 1805. One older brother became a physician; another brother followed the footsteps of his father to develop the paternal locksmith shop into one of the largest industries in Austria, the Skoda works. When Joseph decided to study medicine, his parents were unable to raise sufficient funds and if it had not been for the generosity of a friend who advanced some money, he would have abandoned his plans and taken the monastic habit. He proceeded to Vienna on foot to commence his studies at the University which he later helped to make world-famous. During his student career he was obliged to give private lessons in physics and mathematics in order to pay his way. Thus, through hardships imposed on him because of lack of funds, he acquired knowledge in the fundamental sciences which played no small part in his phenomenal achievements later on. He graduated in 1831 and then returned to his native land, where he attracted immediate attention by his successful management of a cholera epidemic which prevailed there.

Skoda returned to Vienna in 1833 and succeeded in obtaining a subordinate position in the Vienna General Hospital. This was about the time when Rokitansky, Draut and Kolletschka were developing the refinements in pathologic anatomy for which they became known all over the world and it was to them that he attached himself for the next two years. But his interests were really at the bedside, for he reasoned correctly that the knowledge of pathology would serve no good purpose unless it received practical application to the living subject. He was impressed by the studies of Auenbrugger on percussion and of Laënnec

on auscultation but realized that either they were not being utilized at all or they were incorrectly applied. With this background then and his knowledge of acoustics he proceeded to develop the inductive method in medicine through which conclusions are based on well-known physical laws rather than on superficial observation and guesswork. His studies of the cadaver, as well as of the healthy and the diseased body, gave him an understanding of the physical causes of every sound. This made it easier to understand and to teach his subject, a task in which he became so proficient that he soon attracted physicians from home and abroad to his classes and made himself famous as an expert diagnostician of complicated diseases.

Above all, Skoda directed his studies to the auscultation of the heart, noting the cardiac impulse and the origin of heart sounds, striving to localize them with anatomic precision and to distinguish between normal and abnormal heart sounds. It is said that he conducted his bedside investigations with such zeal that he was accused by his patients of "mauling them about," an incident which led to his temporary transference to the "department for mental disorders," where he carried on his work nevertheless.

Eventually in 1839 Skoda published his famous monograph, "Abhandlung über Perkussion und Auskultation," which passed through many editions and was translated into many languages and which constitutes the foundation of modern physical diagnosis:

But these epoch-making teachings did not meet with universal acclaim. From the beginning Skoda ran into strong opposition, especially from the German School. It will be recalled that Piorry, who invented the pleximeter, claimed that every organ had its special sound ("lung sound," "heart sound," "spleen sound," and so forth) and that by use of the pleximeter he was able to determine the thickness of the heart wall and even the exact border between the right heart and the left heart as well as many other extravagant claims. That Skoda's complete rebuttal of Piorry's hypothesis, which put the latter entirely in the wrong, was not accepted with acquiescence is plain to see. Even Skoda's own chief, Hildebrand, at the time of the publication of his monograph ridiculed the views expressed therein. In fact, if it were not for the support of Baron Türkheim, a far-seeing member of the Ministry, Skoda might not have been able to uphold his stand, nor would he have been able to publish his monograph had he not had the protection of the Baron.

Strange to relate, those who flocked to Skoda's lectures were the older practitioners and those from other lands. According to Wunderlich (quoted by Sigerist), "professors, imperial councillors, and practitioners of long standing, animated with an eager determination to learn the mysteries of auscultation and percussion," filled his audiences.

Despite the opposition which prevailed in his own school and probably through the intervention of Baron Türkheim, Skoda obtained in 1840 two wards in the Vienna Hospital devoted to diseases of the thorax. By the next year, he was promoted to be full physician in that hospital, a post which gave full scope for his extraordinary abilities. In 1846 he became professor of clinical medicine, a position that he held until 1871, when he retired because of ill health and suffering caused by gout.

The criticism of therapeutic nihilism which has always been leveled at the School of Medicine of Vienna must be shared by Skoda. Be it said in fairness to this great teacher, however, that his views sprang from his own personal experiences. Originally, he drew blood, leeched and blistered freely and used emetics and mercury, as was the prevailing custom. It was only when he saw the futility, indeed the nocuousness, of such heroic measures that he abandoned them and taught accordingly. In this connection Balfour quoted some interesting statistics with reference to the mortality rate of pneumonia in Skoda's wards, where conservative measures were used, as compared with the Edinburgh Infirmary, which still adhered to the vigorous therapy of the day. Thus in three years and five months 392 patients who had pneumonia were admitted to Skoda's wards with a mortality rate of 13.7 per cent while in five years and three months 253 patients who had pneumonia were admitted to the Edinburgh Infirmary, among whom the mortality rate was 35.9 per cent. Balfour further commented on the method whereby Skoda treated diseases of the heart by rest, diet and innocuous placebos instead of by bleeding and digitalization. If this conservatism practiced by Skoda is to be considered as therapeutic nihilism then by all means let us have more therapeutic nihilists!

Skoda died June 13, 1881. His success was at least appreciated before his death. In 1875 he received the congratulations of all the bodies of learned men in Vienna, a gold medal being struck to commemorate the event. The centenary of Skoda was commented on in an editorial in the British Medical Journal in 1905 as follows: "The work with which Skoda's name will always remain associated is the development of the methods of physical diagnosis which were introduced by Auenbrugger, Laënnec, Piorry and others. Skoda made of percussion and auscultation veritable instruments of precision in diagnosis and his name deserves to rank with those of the actual discoverers of these methods."

REFERENCES

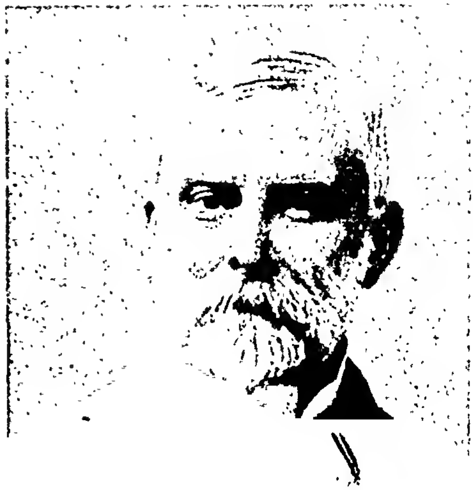
Balfour, G. W.: Notes on the practice of Skoda. Edinburgh M. & S. J. 68:397–405, 1847.

Dawes, S. L. Little biographies; XXXIV. Skoda. Albany M. Ann. 30:199–202, 1909.

Editorial: The centenary of Skoda. Britt. M. J. 2:1551–1552 (Dec. 9) 1905.

Obituary: Hofrath Professor Joseph Skoda. M. Times & Gaz., London. 2:51, 1881.

Sigerist, H. E.: The great doctors; a biographical history of medicine. (Translated by Eden and Cedar Paul.) New York, W. W. Norton & Company, Inc., 1933, pp. 297–302.



SIR THOMAS LAUDER BRUNTON

(1844–1916)

On March 4, 1844, Thomas Lauder Brunton was born at Bowden, Roxburghshire, Scotland, the youngest son of James Brunton, a gentleman farmer. According to the custom of the day, young Brunton received his education by means of private tutors. In 1862, at the age of eighteen years, he entered the University of Edinburgh to pursue the study of medicine. Brunton was an exceptionally good and industrious student and was frequently commended by his teachers. He received the degrees of Bachelor of Medicine and Master of Surgery in 1866 and, a year later, received the degree of Bachelor of Science. The latter degree was granted to Brunton after he had completed successfully a year as house officer at the Royal Infirmary in Edinburgh under the guidance of Professor Hughes Bennett. In 1868, Brunton was awarded a gold medal for his splendid thesis, "Digitalis with some observations on the urine," and he also received his Doctorate in Medicine. Two years later he was granted the degree of Doctor of Science.

Early in his university studies Brunton manifested an unusual interest in drugs and their actions and this interest continued to prevail throughout his entire professional career and was to be the field in which he made his most outstanding contributions. From 1867 to 1869, in addition to participating in research at Edinburgh, he journeyed to the Continent to study at medical centers in Austria, Germany and Holland. Among his teachers were Ernst Wilhelm von Brücke, Isidor Rosenthal, Ludwig Traube, Willy Kühne and Carl Ludwig. Most of the time spent abroad was with Carl Ludwig in his new laboratory at Leipzig where Brunton evidently received additional practical encouragement to con-

tinue in pharmacologic research. While working with Ludwig, Brunton investigated the problem of the independent contraction of arterioles and capillaries in relation to drugs, especially with regard to the actions of amyl nitrite and sodium nitrite. These proved to be the preliminary observations to his later and classic contribution to the use of amyl nitrite in treatment of angina pectoris.

On his return to Edinburgh, Brunton continued his investigations and undertook to study the effects of digitalis on the blood pressure of animals. He utilized a simple column of mercury to determine blood pressure. He also recorded blood pressure by means of the sphygmograph, both on laboratory animals and on human subjects. During his work on patients, Brunton had previously observed that the blood pressure was frequently elevated during the seizures of angina pectoris. These observations, together with his previous experimental work with the nitrites, led to his monumental work, "On the use of nitrite of amyl in angina pectoris," which was published in the "Lancet" in 1867.

In 1870 Brunton went to London to take up residence and in the same year he was honored by his election to the Royal College of Physicians. He became lecturer on materia medica and pharmacology at Middlesex Hospital and the following year he was appointed casualty physician at the famous St. Bartholomew's Hospital. Before the first year at St. Bartholomew's Hospital had expired, Brunton received an important promotion when he was made joint lecturer in materia medica and therapeutics. These lectures were shared with Dr. Frederick Farre until 1875, when Farre resigned and Brunton assumed full charge of the course. Toward the close of 1875 Brunton was appointed assistant physician to the hospital. A year earlier he had become editor of the "Practitioner" at the early age of thirty years.

Brunton completely revised his course of materia medica and therapeutics, basing his instruction on fundamental physiologic principles, and demonstrated the action of drugs on himself, on his students and on laboratory animals. Well-liked by his students and visitors, Brunton was always assured of a large and attentive audience.

In recognition of the high quality of his original research and the brilliance of his teaching, Brunton was elected to fellowship in the Royal Society in 1875. His work up to this time, in addition to his outstanding contribution dealing with amyl nitrite in the arrest of anginal seizures, had been concerned with the physiology of digestion and secretion, with the chemical composition of the blood and with the actions of digitalis and mercury. He was a member of the Council of the Royal Society from 1882 to 1884 and from 1905 to 1906, and served as vice-president of the organization during 1905 and 1906.

Brunton held many important positions during his long and productive professional career. In 1878 the new department for diseases of the

throat was established at St. Bartholomew's Hospital and he was appointed its chief. He held this position for two years, after which the post was assumed by Sir Henry T. Butlin. Brunton became full-time physician to St. Bartholomew's Hospital in 1895 and held this position until 1904, when, owing to illness, he was obliged to resign. The hospital authorities immediately appointed him an honorary consulting physician and a governor of the institution.

Brunton was a kindly and philanthropic man and for many years personally paid the expenses and the salaries of the pharmacologic laboratory at St. Bartholomew's Hospital. For several years he acted as examiner for the Royal College of Physicians and served as a censor from 1894 to 1895. Brunton's profound knowledge of pharmacology and his great ability as a lecturer inevitably led to many invitations to address important medical assemblies. In 1877 he delivered the Goulstonian lecture on "Pharmacology and therapeutics"; a year later, the Croonian lectures on "The connection between chemical constitution and physiologic action." In 1894 he was selected to deliver the Harveian oration and discussed "Some features in the physiology and pharmacology of the circulation."

In 1886 Brunton was appointed to membership on a committee to investigate fully Pasteur's treatment for hydrophobia. Three years later the editors of the "Lancet" invited him to repeat the experiments dealing with the inhalation of chloroform which had been the function of the Second Chloroform Commission at Hyderabad, India, an undertaking which had been sponsored by his Highness, the Nizam.

In addition to holding memberships in the leading medical organizations of Great Britain, Brunton was a member of numerous American societies. He was a member of the American Academy of Arts and Sciences, the Academy of Natural Sciences of Philadelphia, the College of Physicians of Philadelphia and the American Therapeutic Society. He also held memberships in the Therapeutic Society of Paris and the Imperial Academy of Medicine of St. Petersburg.

Brunton was knighted in 1900 and became a baronet in 1908. He received the honorary degree of Doctor of Laws from the Universities of Aberdeen and Edinburgh and the University of Dublin bestowed on him the honorary degree of Doctor of Science.

Brunton was a prolific medical author. One of his most important works was his "Textbook of pharmacology, therapeutics and materia medica," which appeared in three editions between 1885 and 1887. In 1907 his "Collected papers on circulation and respiration" was published. He was an ardent advocate of universal physical and military training and preparedness.

In 1879 Brunton married Louisa Jane Stopford, daughter of Edward A. Stopford, Archdeacon of Meath. There were two sons. The elder,

Major James Stopford Lauder Brunton, succeeded his father in the baronetcy on the latter's death in 1916. The younger son, Dr. Henry Pollock Brunton, was killed in action in France on October 8, 1915. It will be recalled that Sir William Osler's son was also killed in World War I. Lady Brunton died in 1909.

Sir Thomas Lauder Brunton, eminent scientist and teacher, known as the "kindly Scot," died on September 16, 1916, at the age of seventy-two years. He is interred in Highgate Cemetery in London.

REFERENCES

Garrison, F. H.: Sir Thomas Lauder Brunton, M.D. (1844–1916), an apostle of preparedness. Mil. Surgeon. 40:369–377 (Apr.) 1917.

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, pp. 653–654.

MacDougall, J. A.: Obituary. Sir Lauder Brunton, Bart., M.D., C.M., D.Sc. (Edin.), M.D.R.U.I. (Hon.), LL.D. (Edin. and Aberd.), F.R.C.P., F.R.S., consulting physician to St. Bartholomew's Hospital. Edinburgh M. J. n.s. 17: 345–349 (Nov.) 1916.

Obituary: Sir Thomas Lauder Brunton, Bt., M.D., F.R.S., consulting physician to St. Bartholomew's Hospital, London. Brit. M. J. 2:440–442 (Sept. 23) 1916.

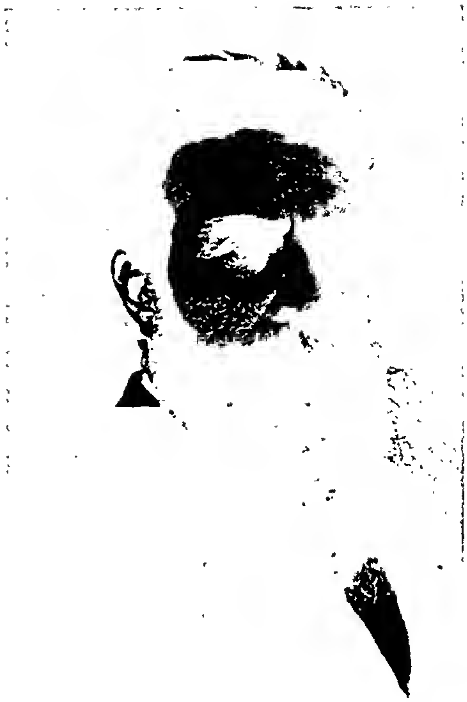
Obituary: Sir T. Lauder Brunton, Bart., M.D., C.M., D.Sc., Edin., M.D.R.U.I. (Hon.), LL.D. Edin. and Aberd. (Hon.), F.R.C.P. Lond., F.R.S., consulting physician to St. Bartholomew's Hospital. Lancet. 2:572–575 (Sept. 23) 1916.

Power, D'Arcy: In memoriam. Sir Thomas Lauder Brunton, F.R.S., 1844–1916. St. Barth. Hosp. Rep. 52:1–9, 1916.

Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors. St. Louis, C. V. Mosby Company, 1941, pp. 557–564.

WILHELM KONRAD ROENTGEN

(1845-1922)



In this biographic commentary the lives and achievements of two great contemporaries will be considered jointly. One lived in Europe, the other in America. Roentgen discovered the x-rays named after him; Williams applied that discovery to establish one of the basic procedures employed in the diagnosis of diseases of the heart.

Wilhelm Konrad Roentgen was born on March 27, 1845, in Lennep in the Rhineland, the son of a German father and a Dutch mother. His childhood was spent in Utrecht, the former home of his mother. An only child, Roentgen received the undivided attention of sensible parents who together materially contributed to his ultimate success.

Roentgen's father, Friedrich Konrad Roentgen, was a simple, reserved and religious man from whom, Hirsch stated, the boy inherited his qualities of industry, patience, directness and perseverance. From his mother he acquired imagination, the desire for the truth in all matters, simplicity and modesty, which comprise the essential characteristics of a true investigator.

His boyhood was spent in an atmosphere of simplicity, thrift and piety. A well-developed and well-proportioned boy, he was inclined toward reticence. Following a few years in an elementary school the decision was reached that he was to become a scientific farmer and he entered the agricultural school at Apeldoorn, Holland. Early in childhood, young Roentgen had manifested unusual interest in nature and its phenomena. He got along well in his studies but was apparently not a brilliant scholar.

About this period of Roentgen's development an incident occurred

which profoundly affected his life for many years. Engaged in a harmless school prank with other boys, he was identified as one of the participants. When he was confronted by the teacher he readily admitted his part but refused to name the other boys. This resulted in his peremptory dismissal from the school and made it difficult to obtain entrance to others. The incident, together with its consequences, was a great disappointment to young Roentgen and his parents because it necessitated a complete revision of their plans. He attempted to pass examinations which would have permitted him to enter a German university, but failed.

Still undaunted in his determination to secure further education, he finally discovered that the Polytechnical Institute in Zurich accepted students without entrance examinations. Accordingly, he entered this school and conscientiously applied himself to his studies. He promptly came under the influence of the great physicist, Clausius, whose teaching and personality inspired young Roentgen to serious efforts. From this illustrious leader Roentgen learned of Clausius' researches on the mechanics of heat production, on the kinetic constitution of gases and on the nature of molecular movement in gases. Although he was not properly registered in the School of Experimental Physics, this very deficiency goaded him to unusual attentiveness and industry, which soon after graduation won him an assistantship with Kundt. Young Roentgen soon became the favorite pupil of Kundt who recognized the great potentialities of his young assistant. At graduation Roentgen received the degree of Doctor of Philosophy from the University of Zurich.

Later, when Kundt was called to the University of Würzburg, Roentgen went with him. At this time he married the woman who was to be his companion for many years. Roentgen's lack of academic credits continued to haunt him and when his teacher attempted to obtain a faculty position for him, the University authorities denied the petition. Almost coincidental with this new disappointment, Kundt received the professorship at the newly founded University of Strasbourg, where the traditions of pedagogy were less strict than at Würzburg, and Roentgen, after two years of assistantship, received the appointment of Dozent in Physics. At the age of thirty years, Roentgen was appointed professor of mathematics at the Academy of Hohenheim, but at Kundt's suggestion resigned this post after a year and accepted the position of associate professor of theoretical physics at the University of Strasbourg.

Roentgen's progress and development were rapid and after three years at Strasbourg he received the appointment of professor of experimental physics at the University of Giessen. He held this position for ten years, teaching and carrying on research, and he frequently remarked that these were the happiest years of his life.

In 1888 Roentgen accepted the professorship of physics at the Uni-

versity of Würzburg, the same university which earlier had denied him an assistantship of minor importance. It was in the Spring of 1895, as director of the Physical Institute at the University of Würzburg, that he made his famous discovery while engaged in working with a little vacuum tube of glass which glowed with an iridescent light. This little tube was the culmination of the efforts of many famous physicists such as Faraday, Plücker, Gassiot, Geissler, Hittorf, Varley, Crookes and Lenard, but to Roentgen, it still contained many mysteries. Geissler had found that when current from an induction coil passed through it, it glowed and flickered with color effects; Hittorf had demonstrated the presence of the cathode ray contained in the tube and Crookes had shown a change in the phenomena when the vacuum was increased to about one-millionth of an atmosphere. At Hertz's suggestion, Lenard had exhaustively investigated the cathode ray. Fascinating as they were, these accumulated facts failed to satisfy the curiosity of Roentgen.

Roentgen was interested in outdoor photography. One day, with an excursion into the country in mind, he placed a loaded photographic plate holder between the pages of a book on his laboratory table so that he would be reminded to take it with him. Somewhere in the book, overlying the sensitized photographic plate, was an antique metal key which was conveniently used as a bookmark. Roentgen was suddenly interrupted in his work and momentarily placed the still-glowing tube on the cover of the book.

The following day he carried out his photographic expedition and made several exposures. When the plates were developed, Roentgen was astounded to find that the shadow of the antique key was imprinted on one of them. At a loss to explain this phenomenon, yet realizing that it was certainly no mere accident, he recollected the events of the previous day. With meticulous care and planning he reconstructed conditions as nearly identical to those of the foregoing day as his memory permitted. After extensive experimentation Roentgen was enabled to photograph the shadows of opaque objects and showed that the structure of bones was revealed by these mysterious radiations. Still perplexed by their unknown nature, he referred to them as the "x-rays."

On December 28, 1895, Roentgen reported briefly regarding his discovery at a meeting of the Würzburg Physico-Medical Society. This work was received with such acclaim that on the completion of his exposition, the Honorary President of the Society, Professor Albert von Kölliker, requested the assembly to designate the new rays as "Roentgen rays." This request was unanimously and enthusiastically approved. In March, 1896, he again appeared reading a paper titled "A new form of radiation." In a third communication (1897) "On further observations of the characteristics of the x-rays," he addressed the Royal Prussian Academy of Science in Berlin.

After spending twelve years at the University of Würzburg, Roentgen somewhat reluctantly accepted the position of director of technical physics at the University of Munich in 1900 and held this post until the spring of 1921. Roentgen was tendered the Presidency of the Royal Physical Institute of Berlin but declined the honor. He received commendation and honors from all parts of the world and the German Government awarded him the Order of the Crown. He received the Barnard medal fom Columbia University and was the first recipient of the Nobel Prize in physics.

At the outbreak of World War I, Roentgen predicted the defeat of Germany and was saddened by the wanton destruction of human life and property. His discouragement was changed to grief when his beloved wife died after a lingering illness. He then resigned his position as director of the Institute of Physics and retired to a lonely life. Roentgen realized that the infirmities of age were making their inroads and expressed the desire to go to his favorite locale and rest in the inspiring environment of the Swiss Engadine region of the Alps, which he so dearly loved. This desire, however, was not fulfilled, for he died after a short illness from a relatively silent carcinoma of the rectum. He passed away at the home of the widow of his old friend, Professor Boveri, in Würzburg and his ashes are in the cemetery at Giessen.

Roentgen's long life was unusually productive. He was primarily a teacher and investigator. His monumental discovery was destined to revolutionize completely the diagnosis and treatment of diseases and to enter and influence many other fields of science.

REFERENCES

Roentgen

Garrison, F. H.: An introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, pp. 721–722.

Hirsch, I. S.: Wilhelm Conrad Roentgen, his life and works. Radiology. 4:63–66; 139–142; 249–253, 1925.

Williams

Brown, Percy: American martyrs to science through the roentgen rays. Springfield, Illinois, Charles C Thomas, 1936, p. 276.

Brown, Percy: Francis Henry Williams, 1852–1936. Am. J. Roentgenol. 36:106–110 (July) 1936.

FRANCIS HENRY WILLIAMS

(1852–1936)

FRANCIS HENRY WILLIAMS was born in 1852 at Uxbridge, Massachusetts, the son of Willard and Elizabeth Dew Williams. He graduated from the Massachusetts Institute of Technology in 1873 and the following year traveled around the world. While in Japan he attended a meeting as an American representative of a scientific expedition.

On his return to the United States, Williams entered Harvard University and graduated in medicine in 1877. The ensuing two years were spent in graduate study in Europe.

Williams established practice in Boston in 1879 and was particularly interested in diphtheria and other communicable diseases. In 1884 he was appointed instructor in materia medica in the Harvard Medical School and later became assistant professor of therapeutics in the same institution. Williams married Anna Dunn Philips of Boston in 1891.

His previous technical training at the Massachusetts Institute of Technology fostered a continued interest in physics and electricity and it is therefore readily understood that he was soon aware of Roentgen's epoch-making discovery. In fact, Williams began his work with the roentgen rays in 1896, only a year after their discovery, while he was attending physician to the Boston City Hospital. As no technical facilities existed at this hospital, Williams' first patients were examined at the Rogers Laboratory of Physics of the Massachusetts Institute of Technology. Finally, the trustees of the Boston City Hospital arranged for facilities in its basement and he worked there until 1915. In 1913, with the establishment of the roentgen-ray department at the hospital, Williams was appointed senior physician.

Williams' promptness in utilizing the new roentgen rays in the examination of patients enabled him to publish one of the first articles on their application to clinical cardiology. This article, "A method for more fully determining the outline of the heart by means of the fluoroscope together with other uses of this instrument in medicine," appeared in 1896. In addition to demonstrating that cardiac enlargement and abnormalities of the cardiac silhouette could be observed by means of the roentgenoscope, Williams emphasized the importance of correlating these observations with physical findings.

With more years' experience, he was able to recognize thoracic aneurysm, pericardial effusion, transposition of the heart, emphysema, pleuritis with effusion, pneumothorax, hydropneumothorax and pulmonary tuberculosis with the aid of the roentgenoscope. In 1899 Williams, collaborating with Walter B. Cannon, demonstrated the physiologic activity of the stomach and intestines.

His comprehensive book, "Roentgen rays in medicine and surgery," was published in 1901 and soon appeared in its second edition.

Collaborating with his friend, Dr. William Rollins, Williams perfected new instruments to make possible the practical use of roentgen rays and radium. He invented the fluorometer, an instrument for the determination of the quantity of roentgen rays given out by the roentgen-ray tube and the quantitative measurement of beta particles (electrons) and gamma rays given off by radium and its radioactive salts. Williams and Rollins improved the roentgenoscopic screen and devised a mechanical stereoscopic roentgenoscope.

Williams received many well-deserved honors and acknowledgments. He was a fellow of the American Association for the Advancement of Science and of the American Academy of Arts and Sciences. In 1917–1918 he was president of the Association of American Physicians. He actively participated in the Massachusetts Medical Society, the American Medical Association and the Société de Radiologie médicale de France. He was a corresponding member of the K. K. Gesellschaft der Ärzte in Vienna and an honorary member of the American Radium Society, the American Roentgen Ray Society and the Radiological Society of North America.

Cognizant of the dangers contingent to exposure to the roentgen rays, Williams early in his work used protective measures and was one of the few pioneers who escaped actinodermatitis and its neoplastic consequences.

Williams retired from active practice in 1930 at the age of seventy-eight years but continued to contribute to the literature of his specialty until his death in 1936. He published a volume, "Radium treatment of skin diseases, new growths, diseases of the eye and tonsils," at the advanced age of eighty-three years.

RUDOLPH MATAS

(1860–)

RUDOLPH MATAS was born on September 12, 1860, at Bonnet Carre, Louisiana, near New Orleans. His father, Dr. N. H. Matas, a native of Spain, was a pioneer ophthalmologist of Louisiana. As with the sons of many doctors, the desire and ultimate determination to pursue medicine as a career was inculcated into the boy at an early age, and wittingly or unwittingly, as the case may be, the paternal influence undoubtedly played at least a subtle role.

Dr. Matas' early education was obtained in various schools in different countries. When only a small boy, he accompanied his parents to Europe, where he attended grammar school in both Paris and Barcelona, Spain. Here he secured his basic proficiency in the languages of France and Spain, which proved to be such an important asset to him throughout his long and productive professional career. On his return to Louisiana, young Matas completed his preliminary education at Brownsville, Texas, and Soules' College in New Orleans and finally entered the Literary Institute of St. John at Matamoros, Mexico, where he graduated in 1876, at the age of sixteen years.

In the autumn of 1877, young Matas entered the Medical School of the University of Louisiana (now Tulane Medical School) and after two years of study, served a two year internship (1878–1880) at the Charity Hospital in New Orleans. Among his teachers were the well-known early Louisiana physicians, Drs. T. G. Richardson, Samuel Logan, A. B. Miles and Edmond Souchon. Dr. Souchon was particularly interested in vascular surgery and contributed widely to the surgical treatment of aneurysm. There can be no doubt that the training and

inspiration derived from this great surgeon profoundly influenced Dr. Matas to embrace this new field of surgery ultimately as his favorite. At the conclusion of his internship, Matas received the degree of Doctor of Medicine in 1880, when only twenty years of age.

Dr. Matas, like others of his generation, lived in the era of surgery when the concepts of antiseptic methods were advocated but disputed and before they were universally accepted. In the following quotation, Dr. Matas recounted this period in his surgical development:

> Thanks to the opportunities given me by my internship, I had ample occasion to acquaint myself with the operations and methods of wound treatment which were in vogue at the hospital at a time when Pasteur's discoveries and Lister's application of them to surgery were still in doubt and dispute, despite the fact that Lister had enunciated the principles of the antiseptic doctrine in 1867, and had continued to accumulate evidence in its favor during the ten intervening years (1867 to 1877).

Dr. Matas began the practice of surgery in New Orleans in 1880. In the early years of his career, his practice was scattered throughout the city. Besides operations conducted at the three existing hospitals, Touro Infirmary, Hôtel Dieu and the New Orleans Sanitarium (which later became the Presbyterian Hospital), he was obliged to perform many operations in the homes of his patients because at this stage in the development of the American hospital the general public still looked on hospitals with grave fear and misgiving.

At the age of thirty-five years, in 1895, Dr. Matas was appointed professor of surgery at his alma mater, where his brilliant teaching career continued uninterruptedly for thirty-two years. Many distinguished surgeons of today owe their training, inspiration and success to the talents, precepts, high intellectual qualities and refinements of this great surgeon and teacher. Since 1928 Dr. Matas has been emeritus professor of surgery at Tulane Medical School. While he is interested and accomplished in all branches of surgery, his greatest interest has been in the development of vascular surgery, in which field he has been an illustrious American pioneer.

As early as 1888, Dr. Matas published his first account of a new method for the surgical cure of aneurysm. He devised the method of intrasaccular suture or "endo-aneurysmorrhaphy," as he termed it, a technic similar to that employed in the closure of intestinal wounds. This article appeared under the title, "Traumatic aneurism of the left brachial artery." In 1902, Dr. Matas gave a detailed description of his operation in an article which was published under the title, "An operation for the radical cure of aneurism based upon arteriorrhaphy."

In the same year Dr. Matas published his experience and that of others in the treatment of aneurysm of the abdominal aorta by the method of wiring and electrolysis (Moore-Corradi method). This method of treat-

ment gained considerable recognition during this era but gradually became abandoned as its uncertainties and limitations became evident.

One of Dr. Matas' outstanding contributions to vascular surgery dealt with his studies and methods of determining the existence and adequacy of the collateral circulation prior to the ligation of a main arterial trunk. By careful methods of compression (the application of a controlled aluminum band) the distal circulation was observed following various degrees of arterial compression. Only when the viability of the tissues supplied by the collateral channels was assured did he proceed with ligation. In 1910 and 1911 Dr. Matas published four articles dealing with the method of determining the adequacy of the collateral circulation. The first article appeared as "Some of the problems related to the surgery of the vascular system: testing the efficiency of the collateral circulation as a preliminary to the occlusion of the great surgical arteries."

Between 1914 and 1924 Dr. Matas wrote extensively on the surgical treatment of arteriovenous fistula and emphasized the serious consequences that occurred when these congenital or traumatic vascular shunts were permitted to exist. In 1924 he reported on the ligation of the abdominal aorta above its bifurcation in the case of a ruptured syphilitic aneurysm involving both common iliac arteries. The patient lived a year and a half following the operation and eventually died as the result of a massive pulmonary hemorrhage from a tuberculous cavity.

Dr. Matas was a pioneer in utilizing nerve-blocking (1898–1899), spinal anesthesia (1899) and laryngeal intubation (1902). From 1888 to 1940 Dr. Matas performed 620 operations on the blood vessels for a great variety of conditions. Few surgeons will ever be granted the opportunity of surpassing this amazing experience. During the same span of years, Dr. Matas contributed 108 articles dealing with the surgery of the vascular system alone.

Many honors and acknowledgments have been awarded to Dr. Matas. He has received LL.D. degrees from Washington University (St. Louis), the University of Alabama and Tulane University; Sc.D. degrees from the University of Pennsylvania and Princeton University; M.D. honoris causa from the National University of Guatemala and the honorary Fellowship of the Royal College of Surgeons of England. Dr. Matas is a Knight of the Civil Order of Alfonso XII of Spain and a Chevalier of the Legion of Honor of France. From 1936 to 1938 he was president of the International Society of Surgery and presided at its meeting in Brussels. Dr. Matas was the Henry Bigelow medalist of the Boston Surgical Society in 1926 and in 1938 was the first recipient of the Distinguished Service Medal of the American Medical Association.

The genuine hallmark of the truly great is the preservation of humility, particularly in the face of well-merited international acclaim. In this

and other respects, Dr. Matas is genuinely one of America's great surgeons, teachers and citizens.

On June 24, 1941, the Board of Managers of Touro Infirmary honored Dr. Matas for his long years of constructive and unselfish service to that institution. At a testimonial banquet a bronze bas-relief plaque of Dr. Matas (sculptured by Mrs. J. Higginson Manning) was unveiled and placed in the Staff Lecture Room of Touro Infirmary and a bronze plate was placed over the operating room, which was named the Rudolph Matas operating room.

At this testimonial banquet various speakers recorded brief quotations from Dr. Matas' writings and utterances of the past which eloquently portray this great surgeon's wisdom, humanity and high standards of culture and intellect. Some of them merit re-inscription in this biography.

* * *

He never lost his human sympathy, his love of his patients, his unsleeping interest in their welfare.

* * *

He had a soul attuned to the finest vibration of human suffering, and a heart that throbbed in unison with human sympathy.

* * *

There is but one road to contentment and happiness, and that is by treading the straight path that is paved with the cement of a clear conscience in the observation of the golden rule, which commands us to deal with our fellows as we would with ourselves.

* * *

The surgeon can never detach himself from the broad pedestal of medicine, or forget that he is first, last and all the time, a physician.

* * *

The surgical scholar must revise and supplement the general knowledge of the fundamental branches, which he has acquired in the under graduate school, by intensive study and laboratory exercises, so that he may be able to apply the data of these sciences to the high differentiated needs of the surgeon.

* * *

It is in the hospital that the *prospective surgeon* comes in contact with the patient, the supreme object of his study and of his laborious scientific preparation. Here he is brought face to face with a conscious human being, a man like himself suffering with all human reactions to pain and distress who appeals to his superior knowledge for relief.

* * *

When we speak of a judicious or wise surgeon, we mean one whose mind is well balanced, one who displays the capacity to weigh evidence quickly, and one who gives a just valuation to the teachings of experience, as well as the facts of science.

* * *

Good judgment is based upon common sense which every normal individual is supposed to possess, but which in reality is far from being a common possession.

The authors of this volume are pleased that they can accord special biographic recognition to a great American physician during his lifetime.

REFERENCES

Garrison, F. H.: An Introduction to the history of medicine; with medical chronology, suggestions for study and bibliographic data. Ed. 4, Philadelphia, W. B. Saunders Company, 1929, p. 733.

Matas, Rudolph: Traumatic aneurism of the left brachial artery. Failure of direct and indirect pressure; ligation of the artery immediately above tumor; return of pulsation on the tenth day; ligation immediately below tumor; failure to arrest pulsation; incision and partial excision of sac; recovery. M. News, Philadelphia. 53:462–466, 1888.

Matas, Rudolph: The treatment of abdominal aortic aneurism by a preliminary exploratory coeliotomy and peritoneal exclusion of the sac, followed at a later sitting by wiring and electrolysis, with the report of two hitherto unpublished cases. Tr. South. S. & Gynec. A. 13:272–330, 1900.

Matas, Rudolph: An operation for the radical cure of aneurism based upon arteriorrhaphy: with the report of four cases successfully operated upon by the author. Tr. Am. S. A. 20:396–430, 1902.

Matas, Rudolph: Some of the problems related to the surgery of the vascular system: testing the efficiency of the collateral circulation as a preliminary to the occlusion of the great surgical arteries; the president's address. Tr. Am. S. A. 28:4–48, 1910.

Matas, Rudolph: Personal experiences in vascular surgery; a statistical synopsis. Ann. Surg. 112:802–839 (Nov.) 1940.

Matas, Rudolph: In: Who's Who in America. Chicago, The A. N. Marquis Company, 1946–1947, vol. 24, p. 1524.

Proceedings of dedication of portrait medallion of Rudolph Matas, M.D.; Chief Surgeon 1907–1935; Emeritus Chief Surgeon 1935. New Orleans, Louisiana, Touro Infirmary, June 24, 1941, 43 pp.

WILLEM EINTHOVEN

(1860-1927)

WILLEM EINTHOVEN was born in May, 1860, in Semarang, Java, of Dutch parents. When he was still a small child, his parents returned to Holland and Einthoven spent the rest of his life in that country. He entered the University of Utrecht in 1879 and received his doctor's degree in 1885 at the age of twenty-five years.

Early in his medical studies, Einthoven manifested unusual interest in the physical sciences and a year after his graduation he published an important paper, "On the law of specific nerve energies," which established his reputation in this field of endeavor. In the same year Einthoven's inaugural thesis was published under the title, "On the influence of color differences in the production of stereoscopic effects." Later in the same year (1886) he was selected as professor of physiology and histology at the University of Leyden. He held this post for the remarkably long period of forty years until death interrupted his active career.

Einthoven's greatest contribution to medicine was his adaptation of the string galvanometer for the recording of the action currents produced by the activity of the heart. He was the true founder of electrocardiography. It will be remembered that the galvanometer was invented by Johannes S. C. Schweigger (1779-1857) of the University of Halle and that Augustus D. Waller in 1887 and 1889 had already recorded the electrical action of the heart by means of the capillary electrometer. Elsewhere in this volume the earlier contributions on electrophysiology by Galvani (1737-1798), by Matteucci (1811-1868),

by von Kölliker and Müller in 1856 and others, have already been mentioned.

Einthoven described the physical principles of the electrocardiogram and designated the deflections of the graph by the letters P, Q, R, S and T. He also made contributions to the other physiologic uses of the method.

Einthoven's classic article, "Die galvanometrische Registrierung des menschlichen Elektrokardiogramm, zugleich eine Beurtheilung der Anwendung des Capillar-Elektrometers in der Physiologie," appeared in 1903. He was responsible for many articles dealing with electrocardiography and in 1913, in collaboration with Fahr and de Waart, postulated his well-known triangle for calculating the electrical axis of the heart. This work appeared under the title of "Über die Richtung und die manifeste Grösse der Potentialschwankungen im menschlichen Herzen und über den Einfluss der Herzlage auf die Form des Elektrokardiogramms."

In calculating the electrical axis of the heart, Einthoven and his coworkers utilized the now historic equilateral triangle, the base of the triangle approximating lead I of the electrocardiogram, the right side of the triangle, lead II and the left side of the triangle, lead III. The electromotive force of the body was represented by an arrow transecting the base and the right side of the equilateral triangle in varying positions. The angle formed by the arrow in its transection of the base of the triangle is the angle of the axis and is obviously variable.

During the instant that the summit of a given deflection is being inscribed in the electrocardiogram, the corresponding axis of potential is not necessarily that of either lead, but this axis can be calculated by means of trigonometric and geometric calculations by use of the equilateral triangle, provided that the potentials of two leads are known.

Since the publication of this important article, Einthoven's triangle and its computations have been extensively used by both clinicians and investigators in the field of electrocardiography.

In 1924, Einthoven received the Nobel Prize in recognition of his valuable contributions to science.

It was the senior author's privilege to meet Professor Einthoven about two years before his death and on his visit to the United States. While this contact was brief it was unusually inspiring and never to be forgotten. Shortly after the word of Einthoven's death reached America the senior author in a short obituary made the following statements: "He exemplified the sterling qualities of a genuine scientist, an indefatigable worker, an earnest, careful investigator, and a gentle and kindly man endowed with that rare quality, humility, which after all, is the stamp of the great. . . . We see the passing of another great man

whose achievements, however, will remain forever as a heritage to the world he so faithfully served."

REFERENCES

Kristenson, Anders: Professor Willem Einthoven. Upsala läkaref. förh. 33:XI–XVI, 1928.

Leaman, W. G., Jr.: The history of electrocardiography. Ann. M. Hist. n.s. 8:113–117, 1936.

Lewis, Thomas: Willem Einthoven, professor of physiology, University of Leyden. Heart. 14:V–VIII, 1928.

Obituary: Willem Einthoven (1860–1927) Dr. Med. Boston M. & S. J. 197:687–688 (Oct. 20) 1927.

Wenckebach: W. Einthoven. Deutsche med. Wchnschr. 2:2176 (Dec. 16) 1927.

Willius, F. A.: Obituary: Professor W. Einthoven. Mayo Clin. Bull. (Nov. 10) 1927, vol. 9.

Winterberg, H.: W. Einthoven. Wien. klin. Wchnschr. 40:1460, 1927.

KAREL FREDERIK WENCKEBACH

(1864–1940)

KAREL FREDERIK WENCKEBACH was born in The Hague on March 24, 1864. His father, Edward Wenckebach, was a prominent engineer who actively participated in the introduction of the telegraphic system into Holland and its extension into the Dutch colonies. His grandfather was a justice of the supreme court in The Hague. A brother of Wenckebach was a landscape artist of note and a son is a gifted sculptor. It is evident that Wenckebach's family background was one of intellectual distinction.

Thus amply equipped with both scientific and cultural endowments, Wenckebach began his studies at the University of Utrecht. He received the degree of Doctor of Medicine in 1888, and that same year was appointed an assistant in the Zoological Institute at Utrecht. Here he carried on many embryologic studies and was also interested in the study of hematology. It was at this time that Wenckebach discovered that he was color blind, which prevented him from working with stained sections. During his tenure at the Institute his important publication, "A treatise on the development of the bone fish," appeared. According to Keith, this work is still referred to by embryologists. Later he published his inaugural dissertation, "The development and structure of the bursa fabricii," for which the Academy of Sciences of Amsterdam awarded him a gold medal. In 1899, he assisted Peckelharing in the publication of a monograph on beriberi.

Wenckebach's realization that he was color blind required him to alter his plans and he decided to embrace ultimately the science of physiology. He married in 1892 and began the practice of medicine in the

village of Heerlen, partly owing to his desire to gain experience in clinical medicine and partly owing to economic reasons. Wenckebach carried out his country practice with zeal and enthusiasm. Among his duties was the supervision of a home for the aged and with these older people under his care he had the opportunity of observing and studying cardiovascular disorders.

On examining a patient one day, Wenckebach became interested by discovering a peculiar cardiac arrhythmia. He remained bent over the patient listening intently for such a long time that the patient thought that Wenckebach had fallen asleep. During his undergraduate days, Engelmann, his former professor of physiology, had demonstrated certain irregularities of the heart beat of frogs. During these early years of his practice, Wenckebach retained close contacts with Engelmann and frequently reported his clinical observations to his former teacher.

In 1898 Wenckebach and Cushny independently demonstrated that in most cases the so-called extrasystoles or ineffectual contractions of the heart were in reality premature beats. Wenckebach's work was so meritorious that in 1901 he was appointed professor of internal medicine and chief of the clinic at Groningen in northern Holland.

Soon Wenckebach began his investigations of the disturbances of cardiac conduction in man. He also conducted experiments with the heart of the dying frog in relation to asphyxia, on the interval between contraction of the ventricles and of the auricles. He demonstrated experimentally that in progressive asphyxia, ventricular contractions can drop out in regular intermissions. He also was able to demonstrate among human beings that such group formations resulted from disturbances of conduction. By means of Mackenzie's records of the arterial pulse, in 1906, Wenckebach demonstrated the first instances of dropped beat when a conduction defect exists. These occasional dropped beats with varying P-R intervals, that is the slowing of auriculoventricular conductivity with periodic dropping of ventricular beats, are known as the Wenckebach periods.

Wenckebach developed a close personal friendship with Sir James Mackenzie and Sir Arthur Keith and this cordial relationship profoundly influenced his future life and work. In 1903, Wenckebach's important monograph, "Arrhythmia as an expression of specific functional disturbances of the heart," which he dedicated to Engelmann, was published in German. An English edition appeared in 1904. Between 1902 and 1905 he published works on the treatment of septic endocarditis, embodying his experiences with colloidal gold therapy. In 1905 he published a small volume on organotherapy.

Wenckebach, in 1907, described a band of muscle fibers in the human heart that arose in the superior vena cava and extended across the sulcus terminalis of the auricle. At that time it was believed that the heart beat

had its origin in the great veins and that this bundle might constitute a conducting path across the sulcus from sinus to auricle. Wenckebach also suggested that the condition now known as auricular fibrillation might be a form of sino-atrial block. A number of pathologists, including Schönberg, examined this bundle in cases in which gross irregularities of the heart beat had been present and widespread inflammatory lesions were said to have been found. Since the actual pacemaker of the heart was later isolated and the nature of auricular fibrillation was recognized, this bundle has lost its original significance.

From 1911 to 1914, Wenckebach served as professor of internal medicine at the University of Strasbourg. It was during this time that he made an important discovery. As early as 1749, Jean Baptiste de Sénac had demonstrated the importance of the use of quinine in the treatment of "rebellious palpitation." According to Wenckebach, many of the older physicians of his era prescribed the combination of quinine with digitalis, because quinine was believed to relieve the disagreeable action of digitalis on the stomach. In 1912, Wenckebach was told by a patient, a merchant from the Dutch East Indies, that when he took quinine for a general tonic he had less trouble with auricular fibrillation than at other times. The patient was able to demonstrate this to Wenckebach's satisfaction. Wenckebach then tried this treatment on other patients but the administration of quinine abolished auricular fibrillation in only a few cases. He did notice, however, that even when he could not abolish this arrhythmia the drug apparently had a quieting effect on the often extremely rapid rate of the ventricle.

The relation of the improvement of the heart action was not overlooked, however. Later, Wenckebach and Frey investigated the effect of the various salts derived from cinchona bark on the heart and found that quinidine sulfate was the most valuable in converting auricular fibrillation into normal rhythm. Wenckebach and Frey found that by administering larger doses of quinine the same results were obtained as by giving smaller doses of quinidine sulfate. Wenckebach also used quinine in combination with strychnine in the treatment of extrasystolic arrhythmia, with marked success. He also reported successful results in the use of quinine in the treatment of paroxysmal tachycardia, sinus arrhythmia, exophthalmic goiter and other forms of hyperthyroidism in which the heart is hyperactive.

In 1914, Wenckebach succeeded von Noorden as the chief of the first medical clinic at the University of Vienna. With the beginning of World War I he undertook a study of the heart in relation to war. He was able to demonstrate that the small heart, which was dependent on an abnormal body habitus, was capable of performing as much work as the heart of normal size. In company with Wagner-Jauregg and Tandler, Wenckebach made a trip to the arena of war and investigated

the effect of location and participation in relation to overstrain and fatigue. Toward the end of the war, Wenckebach and Eiselsberg were summoned to Greece to attend King Constantine, who was ill with empyema. On their return trip they also visited King Ferdinand in Sofia. Later, Wenckebach was called as consultant in the illness of Pilsudski. Many other well-known personages were numbered among the patients of Wenckebach.

During the postwar years, Wenckebach became engaged in the study of malnutrition and its sequelae, which at that time were so prevalent in Austria. The Wenckebach Clinic for the study of rachitic diseases was established in Vienna and, frequently, as many as twenty patients who had rachitis tarda were present at one time. Because of his great interest in malnutrition, Wenckebach was called on to direct the relief work for the nutrition of undernourished children in Vienna. Through his connections in England, Holland and the United States he was able to bring much foodstuff to the impoverished city of Vienna. The articles received included condensed milk, rice, chocolate, fat, conserves, flour and cod liver oil. These articles he personally allotted to children's hospitals and to the many malnourished children.

In 1923, the Thirty-Fifth Congress of Internal Medicine convened in Vienna under the chairmanship of Wenckebach. In 1923 and 1924, he traveled to the United States. Previously Wenckebach had been invited to visit the United States, the invitation having been extended by Sir William Osler during his residence in this country. Wenckebach had been unable to come at that time, a fact which had caused him keen disappointment. He was warmly received in America and traveled extensively, visiting important medical centers, attending medical meetings and delivering numerous lectures. He delivered an interesting address before the Association of American Physicians entitled "What can we learn from America?"

In the meantime, economic conditions improved in Vienna and Wenckebach's clinic flourished. Many physicians from all over the world came to Vienna, as formerly, to study at this Mecca of medicine. With the large increase in practice, Wenckebach was able to study cardiac arrhythmias in large groups of patients. The result of this study was a two volume work in collaboration with Winterberg on "Irregular heart action," published in 1927.

Wenckebach retired from his teaching position in 1929. However, he maintained his large international practice and devoted much of his time to the study of the cardiac changes in beriberi, which had interested him for many years.

Because the nature of the affection of the cardiac musculature in beriberi was a real and immediate danger and because unexpected and sudden death commonly occurred, Wenckebach resolved to find

an answer to the riddle of the beriberi heart. On the invitation of the Queen Wilhemina Jubilee Fund, Wenckebach journeyed to the Dutch East Indies, where beriberi could be studied in all of its stages. From earlier investigations in collaboration with Dr. Aalsmeer of Java in 1927 it seemed possible to conclude that in beriberi, involvement of striated muscle occurred, particularly in the gastrocnemius, soleus and cardiac muscles. The myocardium, owing to the resultant swelling and induration, lost its power of contraction. The right chambers of the heart were enormously dilated but there were few or no changes in the left chambers. This they explained in recognizing that the right chambers dealt with the affluent blood from the veins, the left chambers receiving only as much blood as the impaired right chambers are able to deliver to them. However, the cause of the heart's sudden failure was not solved completely.

In his more exhaustive study of beriberi, Wenckebach was able to demonstrate the enormous dilatation of the right auricle and the conus arteriosus. The curious bulging of the conus arteriosus was found to be a fairly constant accompaniment of the beriberi heart. Even at the incipient state of beriberi the heart was found to be enlarged, and, especially after exercise, revealed extensive pulsations at the left of the sternum as well as a jumpy pulsus celer. The clinical picture was thus well established. Wenckebach surmised that the cardiac changes in the early stage of beriberi were attributable to widening of the arterioles as well as to degeneration of the myocardium. He demonstrated that the use of epinephrine further dilated the periphery of the arterial system and increased the danger of heart failure. Wenckebach advocated, therefore, the use of pitressin (a hormone extracted from the posterior lobe of the pituitary gland) because of its constricting action on the peripheral vessels. Needless to say, Wenckebach was modest in his claims that "its [pitressin] careful use at the bedside may possibly be a means of combatting heart failure."

During his last two and a half years of life, Wenckebach suffered much but accepted his pain philosophically, saying to Hitzenberger that he had received so much pleasure from life that he dared not complain. Cystopyelitis developed with the eventual occurrence of sepsis and Wenckebach died on November 11, 1940.

Sir Arthur Keith expressed the opinion that Wenckebach was the most effective link between the English world of medicine and that which lies outside of it. He lived in a wonderful era of medical progress to which he himself was a generous contributor. Besides his many contributions to medicine, Wenckebach was well known for his love of music. He had been a pupil of the well-known vocal teachers, Stockhausen and the noted Dutch singer Madame Noordeivier.

His many honors included an LL.D. degree from the University of

Edinburgh, the Order of Merit of the Austrian Republic and Fellowship in the Royal Academy of Amsterdam and in the Kaiserliche Akademie der Wissenschaften. He was an honorary Fellow of the Royal College of Physicians of London and of Edinburgh, the Royal Faculty of Physicians and Surgeons of Glasgow and the Royal Society of Medicine.

It is of great interest and of historic importance that two great Dutch scientists were contemporaries and both notably contributed to the knowledge of the heart and its diseases. Wenckebach and Einthoven were both raised in the Dutch tradition; they were both international savants of science and were recognized as such the world over. Among their great admirers were the brilliant cardiologists of the British School, including Mackenzie, Cushny, Lewis, Keith and Allbutt.

REFERENCES

Falta, W.: K. F. Wenckebach zum Gedenken. Wien. klin. Wchnschr. 53:1067–1073 (Dec. 27) 1940.

Keith, Arthur: Prof. K. F. Wenckebach. Lancet. 1:299 (Mar. 1) 1941.

Keys, T. E. and Willius, F. A.: Cardiac clinics. XCV. The achievements of Karel Frederik Wenckebach. Proc. Staff Meet., Mayo Clin. 17:332–336 (May 27) 1942.

Obituary: Prof. K. F. Wenckebach, M.D., Hon. F.R.C.P. Brit. M. J. 1:219 (Feb. 8) 1941.

Ritchie, W. T.: Karel Frederik Wenckebach. Brit. Heart J. 3:141–144 (Apr.) 1941.

Scherf, David: Karel Frederik Wenckebach; 1864–1940. Am. Heart J. 22:852–855 (Dec.) 1941.

SIR JAMES MACKENZIE

(1853-1925)

JAMES MACKENZIE WAS born on April 12, 1853, at the farm of Pickstonhill, Scone parish, in Scotland. Of Highland stock, the Mackenzie family came from the vicinity of Dunkeld in Perthshire on the banks of the river Tay. His father, Robert Mackenzie, and his mother, Jean Campbell Mackenzie, had settled in Scone parish shortly before the birth of their son. James was the third child and the second son. Within sight of his birthplace were the ruins of the abbey of the kings where much of the early history of Scotland had taken place.

Young Mackenzie received his first education at the village school and later attended the grammar school at Perth, which was founded prior to 1153. When only fifteen years of age, Mackenzie left the school and became apprenticed to a chemist. During this tenure, he came in contact with country physicians and from them received his inspiration to pursue medicine as a career. After five years as a chemist's apprentice, young Mackenzie was offered a partnership in the business but he refused this offer because he had firmly resolved to study medicine.

At the age of twenty-one years, Mackenzie entered the University of Edinburgh. Studies as they were presented afforded him considerable difficulty and, as memory played such an important role in the education of the time, the young man developed an inferiority complex and considered himself a dunce. Wilson quoted Mackenzie's own words pertaining to his sense of frustration. "The things that I remember most clearly about my school education, were that I was considered a dunce at most of my classes, and that the subjects in which I did well

were those in which my understanding, rather than my memory, was called into play."

Mackenzie graduated from the University of Edinburgh on schedule, in 1878. This was a memorable year in medical history for it was the time when Pasteur and Lister were waging their heroic battle for the acceptance of the germ theory of disease. Mackenzie applied for a residency at the Edinburgh Royal Infirmary, received the appointment and remained there a year. The following year, 1879, at the suggestion of his former professor of anatomy, Dr. John Brown, Mackenzie accepted an assistantship with Brown and his partner, Dr. William Briggs, at the Lancashire community of Burnley, in England. After a year in the service of these physicians he was offered a third partnership, which he accepted. Mackenzie remained in Burnley for nearly thirty years.

An important but tragic experience, which proved to be the turning point in his career, befell Mackenzie in the early years of his practice. He was attending a young woman in childbirth and from all indications the procedure promised to be a normal and uneventful one. As labor progressed, and apparently without warning, the patient suddenly died and Mackenzie realized that death resulted from abrupt and unanticipated failure of the heart. As he broke the tragic news to the husband, Mackenzie in a sense felt responsible for the death because he had not detected any signs of heart disease. He wondered whether any evidence did exist which had escaped his attention and at that moment he resolved to undertake an intensive study of the heart and its diseases.

He first interested himself in a study of the heart in pregnancy and, in a search of the existent literature on the subject, was disappointed at finding nothing useful or instructive. Mackenzie therefore resolved to find the answers to his questions from a careful study of all patients who came under his care. In pregnant women, as well as in healthy nonpregnant women, he noted changes in the size and position of the heart and studied murmurs, variations in rate and rhythm of cardiac action and other abnormalities.

At this point in his studies, Mackenzie felt the desirability of obtaining more accurate and precise observations than he yet had and turned to the graphic registration of pulse waves, particularly in cases in which irregularity of rhythm occurred. A short review of the historical development of these early recording instruments may be of interest to the reader.

The first polygraph was devised by Étienne-Jules Marey (1830–1904) in 1860 and consisted of an ordinary kymograph drum bearing smoked paper which was arranged to rotate horizontally. Two tambours were attached in such a manner as to inscribe a record on the smoked paper of the drum. The two tambours permitted the simultaneous registration of two waves, such as the waves of the jugular vein and the carotid

artery, or the waves of one of these vessels and the apex beat of the heart. The instrument, however, lacked mechanical precision.

In 1901, V. Jaquet produced a cardiosphygmograph which carried three Marey tambours, the double-jointed levers of which traced records above that of the lever attached to the stylus on the radial artery. The chief objection to this instrument was the difficulty in adjusting and maintaining the contacts with the various positions on the body.

Toward the close of the century, Mackenzie became interested in the use of the polygraph and devised a simple instrument on the general principle of Jaquet's creation. In the following quotation Mackenzie briefly relates the story of his first polygraph:

> In my early days when investigating the action of the heart, I attached a tambour to the upright stem of a Dudgeon sphygmograph in such a manner that I was able to obtain, at the same time as the radial pulse was being recorded, some other movement, as the jugular pulse, apex beat, or carotid. As, however, there was a good deal of inconvenience in the blackening and varnishing the papers, and as it was not possible to get a long tracing upon the heart's rhythm, I discarded this for the ink polygraph.

Later, with the aid of a watchmaker, Mr. Shaw of Padiham, he created the ink polygraph. The recording levers bore ink pens which wrote on a roll of white paper so that long series of tracings could be obtained. This is essentially the same instrument which is still at times used today.

A discussion of Mackenzie's works is given in the main text of the volume and will not be repeated here. His fame spread rapidly and as frequently occurs, Mackenzie was better known abroad than at home. The higher medical circles of England had not yet seen fit to recognize and embrace a "country doctor." After the publication of several of his important works four physicians from Germany visited England with the specific intent of meeting Mackenzie. They were told that no such person existed. These insistent Germans replied that they had read and studied his book and were desirous of meeting this great man. One of them became so irritated by the evasive tactics of the great physicians that he bluntly stated, "We have come here to meet Doctor Mackenzie, and not to meet you. We do not care about you nor your big men, who are all very small men outside your own country."

In 1906, Dr. Arthur F. Hurst, a Radcliffe Traveling Fellow, awakened the medical profession of England following a tour of the Continent by writing an article in the Guy's Hospital Gazette from which the following quotation is extracted.

> Of all English physicians, the best-known and most frequently quoted in Germany is, probably, Doctor Mackenzie of Burnley, a prophet who has hardly met, in his own country, with the recognition he deserves. The methods of studying disorders of the circulation introduced by him are much employed, and many important investigations confirming and extending his results have been published in Germany.

After practicing medicine at Burnley for nearly thirty years, Mackenzie located in London in 1907 when he was fifty-four years of age. The first year his income was only about $600 but he soon became one of the most famous consultants of Harley Street. His acceptance by the Royal College of Physicians inevitably followed and soon thereafter he was honored by receiving a fellowship in the Royal Society and in 1915, received his knighthood.

In 1919, in his book, "The future of medicine," Mackenzie rather bitterly assailed the existing philosophy of some of the so-called elite medical societies of England.

> There has arisen a tradition that only a select body of men are competent to fill a teaching post. This is the result of human frailty. If, in any sphere of life, a few individuals are set apart and given power over their fellows, it is but human that such a select body will seek to aggrandize their position at the expense of their fellows. It is unnecessary to enlarge on this general statement, as the world's history shows its truth in all spheres of human thought and action. In some spheres it may be good, or it may be bad, but in intellectual matters, and especially in science, it can only be bad. In medicine, the teachers have practically taken into their own hands the guidance of education and all the intellectual interests of the profession, and ordain the course a man must follow who wants to become a doctor.
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> We have in London a body—the College of Physicians—which has acquired the power, indirectly, of preventing anyone who is not a member of their body obtaining an appointment as a physician on the staff of a teaching hospital. A young aspirant to such a post must follow certain lines which custom prescribes. He can exclude himself from having any personal contact with patients by spending his time in a laboratory undertaking what is called "research," and this is the surest way of attaining his object. He may spend his time in any other form of academic life, but one method he must not pursue—he must not attempt to qualify himself efficiently for such a post by the experience of general practice. If, for instance, he wishes to see the kind of life his future students would lead, or if he wishes to investigate the early signs of disease, and for that purpose undertakes general practice, he will, by such a step, render himself unfit for membership of the College of Physicians, and so cut himself off from any chance of obtaining a position as a physician to a teaching hospital.
>
> The College of Physicians practically requires of its members that, while they may pursue almost any one of the branches into which medicine is split up, they must not practice medicine in the only way by which a wide outlook may be obtained, and so render themselves fit and capable to become really effective teachers. . . .
>
> One special function of a consultant is to foretell, what is going to happen to a patient if treated, or if left untreated. To obtain this knowledge it is necessary to see patients through the various stages of disease, and this can only be done by the individual who has the opportunity. The College of Physicians thus prevents consultants following the only way in which this knowledge can be obtained. I have known laboratory-trained young consultants actually refuse to see patients regularly lest they should be considered general practitioners. When I have pointed out to them that they can never assess the value of symptoms unless they watch individual cases of disease for long periods, I have found them incapable of recognizing the need for such knowledge.

The length of this important quotation is justified because Mackenzie's sage remarks on this important subject, inscribed over a quarter of a century ago, have singular significance with reference to a peculiar

medical philosophy which still prevails in many portions of the world today.

Mackenzie was somewhat skeptical of the advent of electrocardiography, not because it was a method of precision, but because he recognized the inadequacies of its utilization. He himself had previously introduced methods of precision for registering the beat of the heart and the pulses in arteries and veins. However, he wisely employed these findings to enable him to detect their counterpart by means of physical diagnosis. We believe that if Mackenzie were alive today he would be compelled to restate his following comments. "When I see the modern cardiologist getting his assistant to take an x-ray photograph of the heart and an electrocardiogram, and even a blood pressure reading, and then behold him sitting down to study these reports, I am truly amazed. I never could have realized that the practice of medicine could have become so futile and ineffective."

We are led to wonder how many physicians of this day and age have read this important paragraph of prophetic wisdom?

In 1918, Mackenzie retired from active practice and moved to St. Andrews, Scotland, where he established the Institute for Clinical Research, now known as the James Mackenzie Institute of Clinical Research.

Mackenzie showed his first symptoms of heart disease in 1901, at the age of forty-eight years, when after strenuous exertion there developed a transient paroxysm of auricular fibrillation which he confirmed by pulse tracings. Six years later there developed a slight feeling of constriction in the upper portion of his thorax, occurring only on undue exertion. At the age of fifty-five years, in 1908, Mackenzie experienced his first severe seizure of cardiac pain, which lasted two hours. At irregular intervals thereafter, until the time of his death, he experienced anginal seizures. Forty-eight hours preceding death, Mackenzie experienced severe, recurrent attacks of thoracic pain.

At postmortem examination widespread coronary sclerosis was revealed and an old cardiac infarct was found near the apex of the left ventricle, which undoubtedly occurred in 1908 when he suffered from his first severe, protracted attack of pain. Death occurred as the result of an acute infarct also found in the region of the apex of the left ventricle.

REFERENCES

Waterston, David: Sir James Mackenzie's heart. Brit. Heart J., 1:237–248, 1939.

Willius, F. A. and Keys, T. E.: Cardiac classics; a collection of classic works on the heart and circulation with comprehensive biographic accounts of the authors. St. Louis, C. V. Mosby Company, 1941, pp. 763–800.

Wilson, R. M.: The beloved physician, Sir James Mackenzie. New York, The Macmillan Company, 1926, 316 pp.

SIR WILLIAM OSLER

(1849–1919)

IT WOULD BE difficult, even in a lengthy biography, to keep pace with all the important events and accomplishments surrounding the life and career of William Osler. No other one person has exercised so much constructive influence on medicine in its teaching, in the development of the system whereby it is taught, in its attitude toward research and learning in general as well as on people in almost every walk of life, as did Osler. His was a life so crowded with romance and color, a character so gifted with versatility, graciousness, charm and spiritual integrity that any man who knows him only as the author of the most extensively read textbook of medicine is indeed the loser, for he has learned of only one facet of a many-sided crystal. The portrayal of Osler's life and all that he stood for is recorded in two extensive volumes by Harvey Cushing. Edith Gittings Reid has written a somewhat condensed version of the life of the "great physician." His manifold qualities, interests and activities are further reflected by the tributes written by a score of his friends, associates and former pupils on the occasion of his seventieth birthday.

Pioneer that he proved to be in the development of medical education and research, Osler was born of pioneer stock. His father, a canon of the Church of England, Featherstone Lake Osler, with his wife, Ellen Pickton, settled in 1837 in upper Ontario, to which they had migrated from England. William, the eighth of nine children, was born on July 12, 1849, at Bond Head. He was educated at Dundas, to which his parents had moved in 1857, at Barrie and at Weston, later known as Trinity College School. Here he was influenced by one Father Johnson, Angli-

can priest and naturalist, through whom he met Dr. James Bovell, a teacher in the medical college and medical director of Trinity College School, who spent weekends at Weston with Father Johnson to pursue a common hobby, searching for specimens to be stained and mounted for microscopic study. This was an important phase in the life of young Osler, for, fired by the enthusiasm of Father Johnson, he spent much of his spare time in learning of the lower forms of life and of the mysteries of nature. Years later Osler taught his students to "observe, record, tabulate, communicate," and to "go out among young fellows and learn from them." That he practiced his own philosophy at this early age is evidenced by his first publication while still a medical student, "Christmas and the microscope," in February, 1869, a title which speaks for itself. For Osler had also learned the use and the value of the microscope, an instrument then of great rarity, in his naturalistic pursuits, from Father Johnson. Osler's love for books and for learning is manifest from these years onward. He not only collected books but read everything in sight with profit. There is little doubt, however, that it was his early experience in biologic science which decided more than did anything else, his choice of becoming a physician rather than a clergyman as he had originally planned.

Osler graduated from Trinity College, Toronto, in 1868 and took his medical degree four years later at McGill University. In July of that year he left for Europe with the idea of studying ophthalmology, a plan which he later abandoned. While in Europe he visited London, Berlin and Vienna. Most of this period was spent in the physiology laboratory of University College, London, under Professor Burdon-Sanderson. He conducted a study on "The antagonistic action of atropine and physostigmine on the white blood corpuscles." In May, 1873, he read a paper before the Royal Microscopic Society and shortly thereafter he was elected to its membership. That summer he described the blood platelets as being normal constituents of the circulating blood, a discovery which was enthusiastically acclaimed at his alma mater, McGill University. The findings were presented before the Royal Society by Burdon-Sanderson the following spring.

In 1874, at the age of twenty-five years, he was appointed lecturer on the Institutes of Medicine, then comprising physiology, histology and pathology at McGill University. During the next ten years he was successively pathologist at the Montreal General Hospital, Professor of the Institutes of Medicine in 1875 and full time physician to Montreal General Hospital in 1878. The active scientific work conducted during this period rounded him out as the mature teacher and laid the foundation for his subsequent eminence in his profession. Harvey Cushing, in summing up this period, wrote: "During the short span of years since his McGill appointment he had stirred into activity the slumbering

Medico-Chirurgical Society; he had founded and supported a students' medical club; he had introduced the modern methods of teaching physiology; he had edited the first clinical and pathological reports of a Canadian hospital; he had recorded nearly a thousand autopsies and made innumerable museum preparations of the most important specimens; he had written countless papers." His departure from McGill was not without a great deal of regret but in losing his services, the University profited by the lasting influence he had exerted on the younger men who remained behind.

Osler made several trips to Europe during this period, receiving the M.R.C.P. in 1878 and on each occasion making contacts with distinguished medical leaders, many of them to become his staunch friends in the years that followed. In 1883 Dr. Osler was made a Fellow of the Royal College of Physicians, London, when he was only thirty-three years old.

In 1884 he accepted the chair of Clinical Medicine at the University of Pennsylvania. Howard Kelly, who later followed Osler from Philadelphia to Johns Hopkins, described the circumstances which prevailed at the time when Osler was offered the chair in Philadelphia. That a stranger should be the chosen one to fill this position brought forth the comment about the "old conservative medical center" that "she had actually broken her shackles, thrown traditions to the winds and pulled William Osler down from McGill in Montreal." We might say that the reputation which Osler had already acquired made this choice easy and though he occupied this position for only five years everyone became aware of "fresh, invigorating currents of life and of new activities in the stereotyped medical teachings" of the time.

The power behind the drive which Osler exerted in the field of medical organization and teaching can be better appreciated if we take stock of the situation at the time. True scientific research had stagnated for the greater part of the nineteenth century in North America and, for that matter, in most of the English-speaking world. This, the era of research in pathologic anatomy, saw notable advances being made in Germany, in Austria, in France and other continental centers. Meanwhile, America was busy expanding to the west, its population was growing rapidly, increasing an already extraordinary demand for physicians. The Civil War with all its disruptions was fought and lost and won.

The medical profession meanwhile deteriorated and the old speculative pathologists flourished. Medical schools sprang up all over the country without university connections and in some cases without hospitals. That there were a few isolated and individualistic triumphs during this period is not to be denied. Ephraim McDowell, of Kentucky, who successfully removed a large ovarian tumor in 1809, paved the

way in operative surgery; James Marion Sims, of South Carolina, devised a method for curing vesicovaginal fistula and so became the founder of gynecologic surgery; William Beaumont in 1833 published his observations on Alexis St. Martin, the most fascinating experiment in human physiology ever conducted; in 1843, Oliver Wendell Holmes, of Boston, recognized long before Semmelweis, who incidentally received most of the credit, the infectious and contagious nature of puerperal sepsis; Crawford T. Long, of Georgia, Horace Wells, of Hartford, Connecticut, and William T. G. Morton are names forever to be associated with the development of anesthesia and Austin Flint made his notable contribution describing and explaining the murmur in rheumatic heart disease which still bears his name.

But for the most part interest lay not in true medical progress. A large and profitable practice was the one sure road to professional and social recognition while serious scientific research received neither the prestige of the profession nor the support of the state. And this happened while America, land of opportunity, was developing her natural resources to become the richest country in the world.

But no period in history has been without its dreamers and its idealists. In Baltimore, Maryland, lived a merchant, Johns Hopkins (1794–1873). No educator himself, he made a wish and he made a will. The wish concerned the promotion of education in the State of Maryland; the will was worth $7,000,000. After his death his fortune was equally divided between a projected university and a hospital, both to bear his name, the latter specifically to be closely integrated with the university and to be an auxiliary of the medical school of the university. The evolution of the university, the hospital and its departments and faculties is a story unto itself. By 1889 the medical school was ready to function and in the meantime a remarkable array of talent had been attracted to Baltimore under the wise presidency of Daniel C. Gilman. Welch, Billings, Martin, Remsen and many others were already big names in American education. It was apparent that the position of physician-in-chief, the one to bring the various activities of the medical clinic into proper relation with one another, to link the clinic with other departments of the university, with the profession and the public and with national and international associations of various kinds, was a most difficult one to fill. That the final decision to invite William Osler to this attractive and important position was made only after extensive deliberation is without doubt, but the interview in Philadelphia between Billings, on behalf of the new university, and Osler has an amusing slant to it. In regard to this visit Osler wrote: "Without sitting down, he asked me abruptly: 'Will you take charge of the Medical Department of the Johns Hopkins Hospital?' Without a moment's hesitation I answered: 'Yes.' 'See Welch about the details; we are to open very soon. I am very busy

to-day, good morning,' and he was off, having been in my room not more than a couple of minutes."

The years that followed were monumental years for Johns Hopkins. Osler's arrival in Baltimore marked a turning point in the trend of medical education in the United States and in the reorganization of American medicine.

The productiveness arising out of Osler's activities is something quite phenomenal. His extensive bibliography on medical subjects including his "Principles and practice of medicine" which was first published in 1892, reflects only a fraction of his accomplishments. He taught actively, he carried a tremendous burden in caring for many physicians and clergymen and their families as patients, he was constantly in demand to deliver addresses, he took frequent trips abroad, he stimulated the reorganization of medical societies and study clubs and he attended their meetings. And yet it is said of him that he seldom passed a student or nurse or friend without taking time for a word of greeting or a cheerful chat. And it is also said of him that though grievously overburdened he was never late for an appointment. "Many are always late at a consultation; few miss a train," is a saying which illustrates the importance he attached to punctuality.

On May 7, 1892, Osler was married to Mrs. Samuel Gross, nee Revere, a direct descendant of Paul Revere, of Boston, Massachusetts. They had an only child, Revere Osler. Of Osler's home much has been written for it held a welcome for everyone alike. To his students, as one of them (W. G. MacCallum) related, "it was not a mere house like other houses, but an enchanted palace where we found, without surprise, men of every country whose names we knew from books, all for a time under the spell of his presence in which we floated day by day." In this same home Osler was constantly enlarging his already extensive collection of rare editions of all kinds. There were the old masters, there were books which told of the beginnings of medicine and all related sciences and of the progress through the years and of those who pioneered in their advancement, to say nothing of what came from his own pen. From this same home precious copies were being sent, now to one library or book lover, then to another, as an inspiration to the efforts of those who had already come under his spell.

The extent to which his personal influence stimulated others is well illustrated by Maude Abbott's role in the development of the Pathologic Museum at McGill, including the remarkable collection of congenitally malformed hearts for which she became internationally known. It all came about as the result of a chance remark. "I wonder now if you realize what an opportunity you have?" he pointed out to Dr. Abbott. This was in 1898 on the occasion of a visit to Osler in Baltimore. At

that time much of the valuable pathologic material sat uncatalogued on the shelves of the museum. It became Maude Abbott's task as curator to convert this collection into teaching material by acquiring the clinical data belonging to each specimen and by subdivision into sections so that chiefs of the various departments could collaborate in the development of an attractive and convenient system of museum teaching. In the process of searching for information, Maude Abbott uncovered the three volumes of Dr. Osler's own postmortem notes, clearly and accurately portraying the findings of the numerous necropsies conducted by him during his Montreal days.

Just where Osler found the time for all his activities has always been a mystery even to those who were close to him, but after sixteen years at Johns Hopkins the relentless drive was beginning to tell on him. So when he was offered the Chair of Regius Professor of Medicine at Oxford in August, 1904, he accepted, and assumed his new duties in May of the next year. England, and especially the more tranquil atmosphere of Oxford, had much attraction for him. But according to his habit, he instantly became again a part of the life about him, and in no time at all Osler was in the midst of almost every scientific, literary and civic activity of the new community; his name appeared on nearly every committee concerned with medical and scientific matters in England; he threw all his weight into the adequate development of the basic medical sciences which are taught at Oxford; he conducted clinics at the county hospital, gave the course in the History of Medicine, saw cases for his colleagues, became an ex officio curator of the Bodleian Library, a Delegate to the University Press, the Master of the old Almshouse at Ewelme, continued to write and deliver addresses—the Harveian Oration in 1906, the Linacre in 1908, the Lumleian Lectures before the Royal College of Physicians in 1910, the Silliman lectures at Yale University in 1913 on the occasion of his last visit to America, and many more. The Quarterly Journal of Medicine, the official organ of the Association of Physicians of Great Britain and Ireland, published by the University Press, came into existence owing to his initiative.

And as always, his home was thronged with guests and visitors. The remark was often made that "many visitors to England made a point of two things—seeing Shakespeare's birthplace and calling on Osler at Oxford."

Countless honors were bestowed on Osler. He had been elected to the Royal Society in 1898, he received honorary degrees from a score of universities and in 1911 at the coronation of King George V, he was created a baronet, one of the few honors which gave him pleasure without adding to his duties. In 1914 Osler was elected president of the Bibliographic Society, and five years later he was honored by his elec-

tion to the Presidency of the British Classical Association, a rare distinction for a doctor of medicine to be recognized as a leader among the classical scholars of his day.

The war came as a tragic disappointment to the Osler family but both Sir William and Lady Osler devoted every effort to do what they felt ought to be done, for has history not shown that disease and starvation are deadlier than bullets? So while this war "seems so unnecessary" he was promptly in the midst of a heavy program helping to organize the Army Medical Department. On August 29, 1917, Revere, their only son, was wounded beyond help in the Ypres salient and died later that day in the presence of Dr. Harvey Cushing, one of his father's closest friends, who wrote of his burial, "A strange scene—the great-great-grandson of Paul Revere under a British flag, and awaiting him a group of six or eight American Army medical officers—saddened with thoughts of his father." "A sweeter laddie never lived . . ." is what Sir William said on receiving this heartbreaking news. In a letter to a friend Lady Osler said ". . . I want to tell you that in it all I feel grateful for the years we have had him and rejoice that he did his duty so pluckily. . . ." These troubled times gave little opportunity for relaxation or letdown and, if from external appearances life seemed to continue for the Oslers as before, their hearts were broken.

On July 12, 1919, Sir William celebrated his seventieth birthday. On both sides of the Atlantic his friends had secretly planned a great celebration for him. In the medical world of the English-speaking countries this might well be called Osler's Day, for through the medical journals and through special articles and addresses his friends, in an unprecedented outburst of genuine affection, paid tribute to one whose first thoughts were always for the other fellow.

In December of the same year he contracted bronchopneumonia, from which he did not recover. He died on December 29, 1919.

Miss Minnie Blogg, librarian of the Johns Hopkins Hospital, has made a compilation of Sir William Osler's bibliography. It includes 773 titles, written between 1870 and 1919. For the first twenty years of his medical life the contributions were almost exclusively on biologic, histologic, pathologic and clinical subjects. He wrote extensively on diseases of the circulatory and hematopoietic systems, aneurysms being one of the favorite topics. Many of his writings were admittedly ephemeral but at least they were of great interest at the time.

It is an interesting fact that whoever has commented on Osler's literary style has seldom done so without extensive quotations from Osler's own writing. Osler's acquaintance with the masters of the English language since the dawn of English literature, his knowledge of the Bible, of ancient mythology and of the classics and his deep interest in the evolution of cultural achievements, particularly the history of

medical science, gave him the command of word and of subject which made his writings so pleasantly readable and so clearly understandable.

"Aequanimitas," his volume of addresses covering the period from 1889 to 1903, was the first of a brilliant series of literary contributions. His "Principles and practice of medicine," first printed in 1892, was followed by an array of biographical essays, including essays on Charcot, Beaumont, O. W. Holmes, Bassett (the Alabama student), John Keats, Thomas Dover (the pirate doctor who rescued Alexander Selkirk from the Island of Juan Fernandez), Sir Thomas Browne, Harvey, Fracastorius, Linacre, Servetus, Pasteur, Stensen, Weir Mitchell, Trudeau and many others. Then there was a score of humanistic addresses dealing with the broader aspects and the ethics of medicine such as "A way of life," "Teaching and thinking," "Nurse and patient," "Unity, peace and concord," "The student life," "Bacilli and bullets," and "Science and war."

His address at Oxford on the occasion of his election to the Presidency of the Classical Association, "The old humanities and the new science," was, according to Welch, who happened to be present, "Osler at his best."

Osler's thirst for books, especially the old medical writings and incunabula, was unquenchable. Even during the busy war years, the one great pleasure in which he indulged was the collection of more documents and more books. It was a "cold" day when nothing new was added. It was a great source of delight to Osler that his son, Revere, too had developed such a rare taste in literature and in this he had received all the encouragement that a parent could possibly have given.

The plans that Osler formulated for the cataloguing and the disposition of his vast private library reflect again the purposefulness of his entire existence. To the Medical Faculty of McGill University went the Bibliotheca Osleriana, 7,600 bound volumes including a methodically arranged collection of original texts and documents relating to the basic discoveries, inventions and advances in scientific medicine. It is in the same library that Osler's ashes are preserved in fulfillment of his own wishes. The best of his collection of English literature is in the "Tudor and Stuart Club," founded at Johns Hopkins University, in memory of his son, Revere, and so named "to encourage the study of English literature of the Tudor and Stuart periods."

Special volumes or groups of writings appropriately selected went to the British Museum, the Bodleian Library, Royal College of Physicians, Faculté de Médecine de Paris, Royal Society of Medicine, University of Leyden, Biblioteca Lancisiana in Rome, Botanic Gardens at Oxford, Cambridge University, The Surgeon General's Office in Washington, D. C., and to many institutions scattered over the length and breadth of the North American continent.

As Ruhräh stated the case, "His reward is to have lived to see the seed which he planted grow and mature, to have as his the love, esteem and gratitude of thousands of students and friends, and among these there are none more grateful, more appreciative, than the workers in the medical libraries of this country." To these we can add those on the continents across the seas.

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"Most can raise the flowers now
For all have got the seed."
—Tennyson

REFERENCES

Abbott, Maude E.: The pathological collections of the late Sir William Osler and his relations with the Medical Museum of McGill University. In: Sir William Osler; memorial number. The Canadian Medical Association Journal. July 1920, pp. 91–102.

Blogg, Minnie W.: Bibliography of Sir William Osler, Bart., M.D., F.R.S. In: Sir William Osler, Bart.; brief tributes to his personality, influence and public service. Baltimore, Maryland, The Johns Hopkins Press, 1920, pp. 121–167.

Brown, T. R.: Osler and the Student. In: Sir William Osler, Bart.; brief tributes to his personality, influence and public service. Baltimore, Maryland, The Johns Hopkins Press, 1920, pp. 55–57.

Brush, E. N.: Osler's literary style. In: Sir William Osler, Bart.; brief tributes to his personality, influence and public service. Baltimore, Maryland, The Johns Hopkins Press, 1920, pp. 115–120.

Cushing, Harvey: William Osler, the man. Ann. M. Hist. 2:157–167, 1919.

Garrison, F. H.: Sir William Osler's contributions to medical literature. Ann. M. Hist. 2:184–187, 1919.

Kelly, H. A.: Osler as I knew him in Philadelphia and in the Hopkins. In: Sir William Osler, Bart.; brief tributes to his personality, influence and public service. Baltimore, Maryland, The Johns Hopkins Press, 1920, pp. 107–109.

Malloch, Archibald: Sir William Osler at Oxford. In: Sir William Osler; memorial number. The Canadian Medical Association Journal. July 1920, pp. 51–65.

Reid, Edith G.: The great physician; a short life of Sir William Osler. New York, Oxford University Press, 1931, pp. 66, 196, 249, 257, 275, 284, 285 and 287.

Ruhräh, John: Osler's influence of medical libraries in the United States. Ann. M. Hist. 2:170–183, 1919.

Shepherd, F. J.: Biographical sketch, Sir William Osler, Bart., M.D., F.R.S., & C. In: Sir William Osler; memorial number. The Canadian Medical Association Journal. July 1920, pp. 19–23.

Sigerist, H. E.: William Osler, 1849–1919. In: The great doctors; a biographical history of medicine. (Translated by Eden and Cedar Paul.) New York, W. W. Norton & Company, Inc., 1933, chap. 48, pp. 394–401.

Thayer, W. S.: Osler, the Teacher. In: Sir William Osler, Bart.; brief tributes to his personality, influence and public service. Baltimore, Maryland, The Johns Hopkins Press, 1920, pp. 51–54.

Thomas, H. A.: Some memories of the development of the medical school and of Osler's advent. In: Sir William Osler, Bart.; brief tributes to his personality, influence and public service. Baltimore, Maryland, The Johns Hopkins Press, 1920, pp. 7–18.

SIR THOMAS LEWIS

(1881–1945)

THOMAS LEWIS WAS born in 1881, the son of Henry Lewis, a wealthy and influential mining engineer, of Tynant, Cardiff. During his formative years he was tutored in his parents' home and later attended Clifton College. His clinical education was at the University College, Cardiff, from which in 1904 he graduated, M.B., B.S. Lond., with the University medal and other prizes and D.Sc. from the University of Wales. In 1906 he was appointed to the Staff of the London Chest Hospital, Victoria Park, and in 1907 he received the M.R.C.P., London, and started his consulting practice with rooms in Queen Anne Street. In 1910 he became the first Beit Memorial fellow and commenced the long series of investigations in experimental and clinical research which made him famous. In 1913 he became consulting physician to the University College Hospital, the institution with which he was associated for most of the remainder of his life. In 1916 he abandoned his consulting practice, for now the trend of his career was finally settled by his appointment as the first whole-time research physician to the staff of the Medical Research Council with a ward and laboratories placed at his disposal by the University College Hospital. Later (1937) this was supplemented by a trust fund from the Rockefeller Foundation.

The colorful career of Thomas Lewis needs no detailed exposition. The fruits of his labors speak for themselves. At the age of twenty years while he was at University College he wrote his first series of articles under the direction of Smale Vincent on "Haemolymph glands." These articles are still standard works. Though he had initially established himself as a consulting physician his heart was always in research and

while on the staff of the London Chest Hospital he associated himself with Starling's laboratory. In 1906 he wrote two articles on "The influence of respiration on the arterial and venous pulses." In them he criticized the work of Leonard Hill, who with a generosity which Lewis always remembered with gratitude, not only wrote to say that he agreed entirely with the views expressed by Lewis but also asked him to contribute a chapter on the pulse for his "Recent advances in physiology." This project took Lewis to James Mackenzie, then newly arrived in London. Lewis became a member of a group engaged in the analysis of cardiac irregularities, to which Mackenzie had already applied himself through the medium of polygraphic studies. At this stage Mackenzie was interested in the total and persistent irregularity which reacted in a peculiar fashion to digitalis, later (in 1909) to be recognized by Lewis and independently by Rothberger and Winterberg as auricular fibrillation, and which Mackenzie had erroneously attributed to "nodal rhythm." This notable advance came through the study of cardiac arrhythmias by means of an Einthoven string galvanometer which Lewis had bought at his own expense and which he was permitted to set up in a cellar at the University College Hospital.

Characteristic of Lewis, his researches always produced a multitude of reports, lengthy, not because of verbosity, but because of the wealth of information springing from his tireless and persistent labors. Most of his papers were published in the journal "Heart," of which he was the founder. He was editor of this journal from its inception in 1908 as well as of its successor "Clinical Science" from 1933 until a year before his death. Characteristic also of Lewis was his leadership among his associates in furthering his central purpose of elucidating the problems of clinical medicine as practiced at the bedside. Lewis was a hard taskmaster, brooking no idleness, short cuts or intellectual dishonesty in those who understudied him and worked with him.

The illuminating information that sprang from his long series of experiments concerning the manner of spread of the excitation wave from the sino-auricular node over the rest of the heart needs no further elaboration here. For this work he was elected a Fellow of the Royal Society in 1918. Then came World War I. Lewis, by now recognized as the leading authority in cardiac disease, was invited by the Medical Research Council to take charge of the study of "soldiers' heart," which he later renamed "the effort syndrome." It was this study which so clearly defined the criteria for the diagnosis of organic heart disease. For it he was made C.B.E. in 1920 and knighted a year later. With his usual thoroughness he initiated the follow-up of 1,000 pensioners with organic heart disease, a study which Grant completed ten years later. Few publications reflect the prognostic trends of valvular heart disease better than does this study.

After the war Lewis returned to the laboratory and his electrocardio-

graphic studies, from which eventuated the brilliant explanation of the nature of auricular fibrillation and flutter as a circus movement of the excitatory wave around the mouths of the great veins.

At this point Lewis returned again to the study of the human subject. While he was engaged in the problem of the effort syndrome he had noted the frequency of the phenomenon of dermatographia among the subjects of his study. Recognizing a common pattern of the reaction of the skin to injuries of various kinds in which the capillaries played the major role, he described the now familiar triple response, which he identified as due to release of a histamine-like substance from the cells. These observations regarding the physiology of cutaneous capillaries closely preceded those independently made by Ebbecke, Dale and Richards, and Krogh. Lewis applied this knowledge of vascular physiology to such conditions as Raynaud's disease and acrocyanosis.

Characteristic again of the man, having exhausted one field he proceeded to another. For now followed a series of publications dealing with the consequences of arrested blood flow to the limbs, indicating the differential paralysis of nerves subserving different functions. Furthermore, Lewis and his collaborators were quick to recognize the basic similarity between intermittent claudication and angina pectoris, an observation made by Allan Burns in 1809. His final interest was actually the phenomenon of pain. Pain from the skin, he postulated, is different from deep pain. In the production of cutaneous pain as well as of the more widespread tenderness, he demonstrated the intervention of chemical agents and reasoned that the latter depend on axon-reflexes through fibers not previously known. He named these "nocifensor nerves." The question of referred pain that had so interested Mackenzie years earlier was reopened and work from Lewis' laboratory showed the segmental distribution of pain arising from deep structures.

In order to appreciate fully the influence of Lewis on medical thought and practice it is to be recalled that the cultural scene had been dominated by pathologic anatomy for many decades. The idea that the experimental method could be applied to the analysis of phenomena seen in the sick patient was viewed with skepticism by his contemporaries. Indeed he ran headlong into strong opposition during the early phases of his career. That he succeeded must be attributed to a tenacity of purpose so insistent that once he set his mind on a project it was only a matter of time before its completion. The peculiar importance of his life lay not so much in the extensiveness of his scientific publications (more than 230 scientific papers and twelve monographs and textbooks of high standard) as in his capacity to visualize the need for applying the methods of science and the critical standards of science to the study of disease in man and in actually bringing this to pass. As Paul White, one of the many American physicians who studied under Lewis, has it, Lewis was "a physiologist in the clinic and a clinician in

III

THE CHRONOLOGIC PRESENTATION OF DATA ACCORDING TO SUBJECTS

I. ANATOMY OF THE HEART AND CIRCULATION

3000–2500 B.C.	Imhotep (?) (ancient Egypt) (Edwin Smith Surgical Papyrus, discovered in 1862), observed the heart as a central organ in the thorax from which vessels were distributed to various parts of the body. Listed twenty-two vessels. (See pages 6, 7.)
Circa 1550 B.C.	Author unknown (ancient Egypt) (Ebers Papyrus, discovered in the winter of 1872–1873). The same observations were inscribed as recorded in the Edwin Smith Surgical Papyrus. In addition to the twenty-two vessels listed in the preceding manuscript, fifty additional vessels were mentioned. (See pages 7, 8.)
14th century B.C.	Nebsext (?), healer, priest or physician (ancient Egypt) (Brugsch or Greater Berlin Papyrus, believed to be the first of the three mentioned papyri to be discovered), gave a description of the heart and vessels virtually identical with that of the Edwin Smith Surgical Papyrus and the Ebers Papyrus. The anatomy of the veins was mentioned. (See page 8.)
1123–256 B.C.	Author unknown. Ancient China. The principal medical work was Nan Ching, which dealt with the arterial and visceral systems. Also recorded the weights of various organs, including the heart. (See pages 9, 10.)
Circa 1000 B. C.	Author unknown. Ancient China. A medical work, Neiching, stated that the liver stored the blood (soul), the heart stored the pulse (spirit), the spleen stored the nutrition (thought), the lungs stored the breath (energy) and the kidneys stored the germ principle (will). (See page 10.)
Circa 500 B.C.	Alcmaeon of Crotona (ancient Greek colony) distinguished the veins from the arteries and is believed to have been the first to practice anatomic dissection. (See page 11.)
5th and 4th centuries B.C.	Hippocrates (460–370 B.C.) of Cos in an anatomic treatise described the cardiac valves, the ventricles of the heart and the great vessels. (See pages 11, 12.)
4th century B.C.	Aristotle (384–322 B.C.) was the originator of comparative anatomy. He did not dissect the human body but carried out extensive dissections on animals. Aristotle named the aorta. He presented a fairly accurate description of the branches of the great veins and the superficial vessels in the forelimbs of mammals. Aristotle believed that the number of ventricles comprising the heart varied with the size of the animal. (See pages 12, 13.)
4th and 3rd centuries B.C.	Erasistratus (310–250 B.C.) of Alexandria predicted the existence of communications between the veins and arteries (capillaries) but erroneously stated that the blood flows from the veins to the arteries. He described the aortic and pulmonary valves and the chordae tendineae. (See pages 13, 14.)
2nd and 3rd centuries A.D.	Claudius Galen (138–201 A.D.) of Pergamon described his fantastic and erroneous concept of the heart and blood

1544	Guido Guidi (Vidius) (d. 1569), of Florence, Paris and Pisa, disproved Galen's contention of the existence of "invisible pores" in the interventricular septum and therefore probably had some notion regarding the presence of the pulmonary circulation, although he made no statement to this effect. (See pages 39, 40.)
1545	Carolus Stephanus (Charles Estienne) (circa 1500–1564), a prominent French anatomist, described the valves of the veins and referred to them as "apophyses membranarum." (See page 40.)
1553	Michael Servetus (1509–1553), of Villanueva de Sigena, Spain (the martyr), discussed the existence of the pulmonary circulation. (See page 40.)
*1556**	Sylvius (Jacques Dubois) (1478–1556), of Paris, in his work "Isagoge" published soon after his death, named the jugular, subclavian, renal, popliteal and other vessels. He also mentioned the valves of the veins. (See page 42.)
1559	Matteo Realdo Colombo (Columbus) (1516?–1559), of Cremona, denied the existence of "invisible pores" in the interventricular septum. He conceived the pulmonary circulation in part but held the view that the nutritive blood was conveyed by the veins. (See page 42.)
1562	Gabriele Fallopio (Fallopius) (1523–1562), of Ferrara, Pisa and Padua, verified many of Vesalius' anatomic discoveries and demonstrated the coronary vessels by dissection. He described a nerve plexus in the heart. (See pages 42, 43.)
1563	Bartolommeo Eustachi (Eustachius) (1524–1574), of Rome, described the pulmonary veins. (See page 43.)
1571–1593	Andrea Cesalpino (1519 or 1524–1603), of Arezzo and Pisa, by means of dissection, observation and logical deductions conceived the general scheme of the circulation of the blood. (See pages 43, 44.)
Circa 1571	Hieronymus Fabricius (1537–1619), of Padua, described the valves of the veins but stated erroneously that their mouths were always directed toward the heart. (See pages 44, 45.)
16th century	Giulio Cesare Aranzio (1530–1589), of Bologna, discovered the ductus arteriosus (frequently attributed to Botalli). He also discovered the corpora Arantii in the heart valves. (See page 45.)
1586	Arcangelo Piccolomini (1525–1586), of Ferrara, correctly described the structure and function of the valves in the jugular veins and the veins of the extremities. (See page 45.)
1628	William Harvey (1578–1657), of Folkestone and London, in his masterly work, "Exercitatio anatomica de motu cordis et sanguinis in animalibus," described both the anatomy and the general physiologic principles of the systemic and pulmonary circulations. He predicted the existence of the capillary circulation. Harvey is generally

* Posthumous publication.

	injection-corrosion method. He contended that anastomoses between coronary arteries did not exist. (See pages 150, 151.)
1893	Wilhelm His, Jr. (1863–1934), of Leipzig and Berlin, published his findings on the histology of the junctional region of the heart. He believed that he had demonstrated a bundle of specialized tissue bridging the auricles and ventricles, the auriculoventricular bundle or bundle of His. (See pages 200, 201.)
1893–1914	A. F. Stanley Kent (1863–), of England, demonstrated the existence of accessory muscular connections between the right auricle and ventricle in various animals (the bundle of Kent). (See page 201.)
2nd half of the 19th century	Karel Frederik Wenckebach (1864–1940), of Groningen and Vienna, described a band of muscle fibers in the human heart in the sulcus terminalis of the right auricle, which he surmised might represent a path of conduction from the sino-atrial node to the auricle. (See pages 229, 230.)
1906	Sunao Tawara (1873–), a Japanese working in Germany, discovered and described the auriculoventricular node (node of Tawara). (See page 232.)
1907	Sir Arthur Keith (1866–), of London and Aberdeen, and Martin William Flack (1882–1931), of London, discovered and described the sino-atrial node (node of Keith and Flack.) (See pages 232, 233.)
1911	Franklin Paine Mall (1862–1917), of Belle Plaine, Iowa, and Baltimore, demonstrated the scroll-like arrangement of the musculature of the ventricles. He demonstrated two distinct spirals, the one coursing from the tricuspid or sinus portion of the heart to the apex of the right ventricle (sinospiral) and the other from the aortic and mitral region to the apex of the left ventricle (bulbospiral). (See pages 244, 245.)

1785	John Hunter (1728–1793), of London, devised and performed his famous operation for aneurysm, which consisted in ligation of the artery at a point beyond the dilatation. However, Jacques Guillemeau had performed this procedure in 1594 and Dominique Anel had also applied the single ligature in 1710. (See pages 91, 92.)
1796	John Abernethy (1764–1831), of London, was the first to ligate the external iliac artery for aneurysm. In 1809 he reported four cases in which the procedure had been employed, twice with success. In 1798 Abernethy ligated the common carotid artery for hemorrhage. (See page 94.)
1801°	Pierre-Joseph Desault (1744–1795), of Paris, was another pioneer in the surgical treatment of aneurysm. He advocated the distal ligation of aneurysms. (See page 107.)
1804	Antonio Scarpa (1747–1832), of Venice, Modena and Pavia, contended that the intima and media of arteries were ruptured in aneurysms. (See pages 107, 108.)
1808	Sir Astley Paston Cooper (1768–1841), of Norfolk and London, successfully ligated the common carotid and the external iliac arteries for aneurysm. Nine years later he performed the then unbelievable feat of ligation of the abdominal aorta. (See page 109.)
1809	Allan Burns (1781–1813), of Glasgow, described unilateral paralysis of the diaphragm resulting from pressure on the phrenic nerve by a thoracic aneurysm. (See pages 109, 110, 111.)
1815	Joseph Hodgson (1788–1869), of Birmingham, gave the best descriptions of aneurysms up to this time and recorded the most accurate description of aneurysmal dilatation of the arch of the aorta. (See page 114.)
1st half of 19th century	Thomas Hodgkin (1798–1866), of Tottenham and London, described and illustrated aneurysms and aneurysmal dilatation of the aorta. (See pages 117, 118.)
1818–1837	Valentine Mott (1785–1865), of Long Island, New York, ligated the innominate artery for the first time in 1818 but the operation was not successful. In 1827 he successfully ligated the common iliac artery at its origin, the carotid artery for aneurysm in 1829, the carotid artery for hemangioma in the same year, the external iliac artery for femoral aneurysm in 1831, the right subclavian artery in 1833, both carotids simultaneously in 1833 and the right internal iliac artery in 1837. All told, Mott ligated great arteries for aneurysms 138 times. (See page 120.)
1819	René-Théophile-Hyacinthe Laënnec (1781–1826), of Paris, was one of the pioneers in the clinical recognition of thoracic aneurysm. (See pages 115, 116.)
1829	Sir Dominic John Corrigan (1802–1880), of Dublin, emphasized the value of auscultation in the clinical recognition of aneurysm of the thoracic aorta. (See pages 122, 123.)
1830	Alfred-Armand-Louis-Marie Velpeau (1795–1867), of Paris, was the first to attempt to obliterate the sac of an

° Posthumous publication.

described the tracheal tug as a valuable diagnostic sign in thoracic aneurysms. (See pages 184, 185.)

1879 Pietro Burresi (1822–1883) and G. Corradi (1830–1907), of Italy, applied the wiring method of Moore and Murchison (1864) in the treatment of aneurysm and passed an electric current through the wire to produce mural thrombosis. This method of electrocoagulation became known as the Moore-Corradi method. (See pages 188, 189.)

1902 Rudolph Matas (1860–   ), of New Orleans, is an American pioneer in surgery of the vascular system. In 1888 he published his first account of a new method for the surgical cure of aneurysm. However, the first comprehensive account of the new method, "endo-aneurysmorrhaphy" or "intrasaccular suture," appeared in 1902. Dr. Matas is the author of 108 important articles dealing with surgery of the vascular system. (See pages 225, 226.)

fibrillation, which they referred to as "pulsus irregularis perpetuus." By means of venous pulse tracings, Rothberger and Winterberg demonstrated that the waves of auricular activity were absent and that the phlebogram showed the positive or ventricular form of venous pulse. Their records were identical with the experimentally produced curves of auricular fibrillation (Vorhofflimmern) (See page 239.)

1909 Sir Thomas Lewis (1881–1945), of London, clarified many of the existent problems concerning auricular fibrillation. He demonstrated its frequency in man and showed it to be the arrhythmia commonly present in mitral stenosis. Lewis concisely described the electrocardiographic characteristics of auricular fibrillation. In 1920 and 1921, Lewis and his students demonstrated the mechanism of circus movement in auricular fibrillation and flutter. (See pages 241, 242.)

1911 W. A. Jolly (1877–1939) and W. T. Ritchie (1873-), of England, made important contributions to the better understanding of auricular flutter and named the disorder. (See pages 238, 239.)

1917 George Canby Robinson (1878–), of Baltimore and St. Louis, in collaboration with J. F. Bredeck, reported the first instance of ventricular fibrillation in man with temporary cardiac recovery. (See page 252.)

of blood in the pleural and pericardial cavities and enlargement of the heart. (See pages 86, 87.)

18th century	Matthew Baillie (1761–1823), of London, demonstrated that palpable pulsations of the abdominal aorta were not indicative of disease. (See pages 92, 93.)
19th century	Jean-Nicolas Corvisart (1755–1821), of Paris, observed that an increased area of precordial pulsation occurred with cardiac dilatation. He translated Auenbrugger's book on percussion and extended the use of the method. (See pages 108, 109.)
1814–1817	Friedrich Ludwig Kreysig (1770–1839), of Berlin, called attention to the systolic retraction of the left half of the epigastrium as a sign of pericardial adhesions. (See pages 113, 114.)
1819	René-Théophile-Hyacinthe Laënnec (1781–1826), of Paris, invented the stethoscope and introduced auscultation. (See pages 115, 116.)
1824	René-Joseph-Hyacinthe Bertin (1767–1828), of Paris, described valvular vegetations and valvular deformities with special reference to their signs and described the presystolic murmur of mitral stenosis. (See page 124.)
1828–1829	Thomas Hodgkin (1798–1866), of Tottenham and London, called attention to the to-and-fro murmurs of aortic insufficiency and commented on the full bounding pulse, stating that at times the patient's head was seen to move in concert with the beat of the heart. (See pages 117, 118.)
1828	Pierre-Adolphe Piorry (1794–1879), of Poitiers, attempted to improve Auenbrugger's method of percussion. He invented the pleximeter but this method of percussion never became adopted universally. (See pages 118, 119.)
1831	James Hope (1801–1841), of Edinburgh and London, described the physical signs of aortic, mitral and pulmonary valvular stenosis and aortic insufficiency. He also postulated the signs that should attend stenosis of the tricuspid valve and described the systolic murmur of mitral insufficiency. (See pages 121, 122.)
1832	Sir Dominic John Corrigan (1802–1880), of Dublin, discussed the origin of the diastolic murmur and clearly described and discussed the characteristic bounding or "water-hammer" pulse of aortic insufficiency, which even today is frequently referred to as the "Corrigan pulse." A year later he criticized Laënnec's interpretation of the physical phenomena designated by the latter as "bruit de soufflet" and "frémissement cataire." Corrigan contended that they were not the result of spasm but resulted from organic valvular changes. (See pages 122, 123.)
1835	Jean-Baptiste Bouillaud (1796–1881), of Angoulême and Paris, described the split-second heart sound and attributed it correctly to asynchronism in closure of the aortic and pulmonary valves. He described the "bruit de diable," a venous humming sound heard over the internal jugular vein in chlorosis, and the "bruit de rappel," which represented the false reduplication of the second sound at the apex in mitral stenosis. (See pages 124, 125, 126.)

Potain recorded arterial blood pressure and demonstrated that hypertension is responsible for the frequently observed cardiac hypertrophy in Bright's disease. (See pages 161–163.)

1868 Heinrich Irenaeus Quincke (1842–1922), of Berlin and Kiel, was the first to make detailed studies of the capillary pulse and to note its significance in the diagnosis of aortic insufficiency. (See pages 163, 164.)

1871 Ludwig Traube (1818–1876), of Berlin, presented a concise description of pulsus bigeminus, its mechanism and significance. He concluded that the phenomenon occurs with failure of the left ventricle and cited an instance in which digitalis apparently contributed to its appearance. (See pages 168, 169, 170.)

1873 Adolf Kussmaul (1822–1902), of Heidelberg, Erlangen, Freiburg and Strasbourg, extensively investigated mediastinopericarditis (adherent pericarditis) and described the "pulsus paradoxus" as a sign at times present in this disease. (See pages 173, 174.)

1876 Sir William Richard Gowers (1845–1915), of London, was one of the pioneers in the use of the ophthalmoscope and studied the retinal vessels in Bright's disease. In studying the ocular fundi of patients who had Bright's disease he confirmed his impressions of the coexistence of hypertension (determined by means of palpation of the radial pulse) with vascular changes in the retina. (See pages 177, 178.)

1876 and 1878 Étienne-Jules Marey (1830–1904), of Paris, was a pioneer in the study of blood pressure and the creator of a sphygmograph. He devised the first reasonably useful apparatus for estimating arterial blood pressure in man. Marey stated that the maximal pressure (systolic) may be determined as the point where the pulsation disappears and the minimal pressure (diastolic) as the point where the oscillations are of greatest magnitude. Marey demonstrated the fundamental fact that the maximal excursion of the pulse wave was obtained when the pressure about the artery was equal to the pressure within the artery. He also devised a sphygmograph with two tambours so that two simultaneous pulse records could be obtained. (See page 178.)

1878 Thomas Morgan Rotch (1849–1914), of Philadelphia, described the absence of resonance in the fifth right intercostal space, known as Rotch's sign, as an early sign of pericardial effusion. (See pages 182, 183.)

1878 William Silver Oliver (1836–1908), of Halifax, Nova Scotia, and later of various points in the British Empire, described the tracheal tug as a valuable diagnostic sign in thoracic aneurysm. (See pages 184, 185.)

1887 Ritter (Samuel Sigfried K.) von Basch (1837–1905), of Germany, introduced the most accurate apparatus yet devised for recording arterial blood pressure in man. He, however, recorded and studied only the systolic pressure. (See pages 190, 191.)

1888 Graham Steell (1851–1942), of Manchester, described the diastolic murmur of pulmonary regurgitation which

garding the degree of existing hyperthyroidism. (See pages 251, 252.)

1920 Harold Ensign Bennett Pardee (1886-), of New York, presented the first detailed description of the changes in the T waves of the electrocardiogram occurring in sudden obstruction of the coronary arteries. (See pages 255, 256.)

at times accompanies the increased intrapulmonary pressure associated with mitral stenosis. This murmur is still known as the "Graham Steell murmur." (See page 195.)

1891–1896	Scipione Riva-Rocci (1863–1937), of Italy, developed the mercury sphygmomanometer which, in principle, was the model for those in present-day use. His work represented the true origin of modern determinations of blood pressure. (See page 199.)
1895	Wilhelm Konrad Roentgen (1845–1922), of Strasbourg, Giessen, Würzburg and Munich discovered the x-rays. The discovery affected every branch of medicine profoundly. (See pages 201, 202.)
1896	William Ewart (1848–1929), of London, described an area of percussion dullness at the left posterior base of the thorax which he believed was pathognomonic of pericardial effusion. This finding is known as Ewart's sign. (See page 202.)
1896	Francis Henry Williams (1852–1936), of Boston, the year after Roentgen's discovery of the *x*-rays, published a classic pioneer study on the use of this new method of examination with regard to the heart, aorta and lungs. (See pages 204, 205.)
1902	Friedrich H. L. Moritz (1861–1938), of Germany, introduced the method of orthodiagraphy. By utilizing the roentgenoscope, he traced the shadows cast by the heart and great vessels on a thin sheet of paper. (See page 227.)
1903	Willem Einthoven (1860–1927), of Leyden, adapted the string galvanometer for recording the action currents of the heart. His demonstration established the science of electrocardiography. Einthoven made many important contributions to this new field. (See pages 228, 229.)
1908	William Sydney Thayer (1864–1932), of Milton, Massachusetts, and Baltimore, described the third heart sound. He believed that it is caused by the first rush of blood into the ventricles from the auricles, during diastole, the impact of which sets the flaps of the auriculoventricular valves in vibration. (See pages 235, 236.)
1909	Sir William Osler (1849–1919), of Canada, the United States and England, described the evanescent painful embolic subcutaneous nodules pathognomonic of the disease now known as "subacute bacterial endocarditis" (Osler's nodes). (See pages 239, 240.)
1914	Alfred Einstein Cohn (1879–), of New York, was apparently the first to describe the effect of digitalis on the T waves of the electrocardiogram. He inferred that the graphic changes resulted from an alteration in the contractile substance of the heart. (See pages 250, 251.)
1915	Henry Stanley Plummer (1874–1936), of Rochester, Minnesota, extensively discussed the blood pressure and pulse changes occurring in exophthalmic goiter and adenomatous goiter with hyperthyroidism. He showed how these alterations could be used in the diagnosis of the disorders and how their proper interpretation gave information re-

garding the degree of existing hyperthyroidism. (See pages 251, 252.)

1920 Harold Ensign Bennett Pardee (1886–), of New York, presented the first detailed description of the changes in the T waves of the electrocardiogram occurring in sudden obstruction of the coronary arteries. (See pages 255, 256.)

V. CONGENITAL MALFORMATIONS AND THE EMBRYOLOGY OF THE HEART AND CIRCULATION

4th century B.C. — Aristotle (384–322 B.C.) was apparently the first embryologist. He studied the development of the chick embryo day by day, described the punctum saliens, observed the fetal heart beat and noted the vitelline and allantoic veins. (See pages 12, 13.)

1493 — Alessandro Benedetti (1460–1525), of Padua, described what appears to be the first recorded instance of malposition of the heart (dextrocardia?). (See pages 32, 33.)

Circa 1571 A.D. — Hieronymus Fabricius (1537–1619), of Padua, contributed to the science of embryology when he studied the formation of the chick in the egg. (See pages 44, 45.)

16th century — Guilio Cesare Aranzio (1530–1589), of Bologna, discovered the ductus arteriosus of the fetus. (See page 45.)

1586 — Arcangelo Piccolomini (1525–1586), of Ferrara, described the foramen ovale and the general conformation of the fetal heart. (See page 45.)

1593 — Giambattista Carcano (1536–1606), of Ferrara, described the course of the vessels of the fetus and also described the ductus arteriosus and the foramen ovale. (See page 45.)

1640 — Pierre Gassendi (1592–1655), of Champtercier, France, described the foramen ovale in an adult. (See page 57.)

1749 — Jean-Baptiste de Sénac (1693–1770), of Versailles, recorded observations on congenital cardiac defects. (See pages 81, 82.)

18th century — Albrecht von Haller (1708–1777), of Bern and Göttingen, demonstrated that the heart of the chick embryo pulsated before any other structure manifested evidence of dynamic function. (See pages 83, 84, 85.)

1761 — John Baptist Morgagni (1682–1771), of Bologna, Padua and Venice, described congenital cardiac defects. (See pages 85, 86.)

1762 — William Hunter (1718–1783), of Glasgow and London, recorded accounts of congenital cardiac defects. He expressed the belief that pulmonary stenosis accounted for multiple defects. (See pages 82, 83.)

1777 — Lazaro Spallanzani (1729–1799), of Scandiano, investigated the role of the heart and circulation from the embryo to the adult. He made extensive observations of the circulation in embryos. (See page 89.)

1777 — The first description of the combination of congenital defects now known as the "tetralogy of Fallot" was recorded by Edward Sandifort. (See page 90.)

1788 — Matthew Baillie (1761–1823), of London, described a case of congenital dextrocardia with complete situs inversus viscerum. He also observed and described transposition of the great arterial trunks in which the aorta issued from

the right ventricle and the pulmonary artery from the left ventricle. (See pages 92, 93.)

1809 Allan Burns (1781–1813), of Glasgow, described six basic types of congenital cardiac anomalies: cases in which the aorta arises from both the right and the left ventricles; those in which the foramen ovale and the ductus arteriosus are open; those in which the ductus arteriosus is closed but the foramen ovale is patent or a defect in the interventricular septum is present; those in which the pulmonary artery is closed at its origin but some blood gains entrance into the vessel from a patent ductus arteriosus; those in which the heart consists of only two chambers, and those in which congenital stenosis of the mitral valve occurs. (See pages 109, 110, 111.)

1814 John Richard Farre (1774–1862), of Glasgow, Aberdeen and London, was another observer to describe the anatomic disarrangement consisting of pulmonary stenosis, dextroposition of the aorta, defect of the interventricular septum and hypertrophy of the right ventricle. This combination of defects today is known as the "tetralogy of Fallot." (See page 113.)

1824 Élie Gintrac (1791–1877), of France, also recorded the description of the combination of congenital cardiac anomalies later to be known as the "tetralogy of Fallot." (See page 116.)

1831 James Hope (1801–1841), of Edinburgh and London, attempted to classify the symptoms and signs of congenital anomalies of the heart. (See pages 121, 122.)

1836 and 1841 Jean-Baptiste Bouillaud (1796–1881), of Angoulême and Paris, expressed the opinion that congenital cardiac anomalies were caused both by inherent defects of development and by disease of the fetus. (See pages 124–126.)

1866 Thomas Bevill Peacock (1812–1882), of London, compiled the most complete volume up to this time dealing with congenital malformations of the heart. He favored the belief that cyanosis in congenital heart disease resulted from venous stasis rather than from the admixture of venous and arterial blood. (See page 159.)

1875 Carl Rokitansky (1804–1878), of Vienna, contributed his classic work on the origin and nature of congenital defects of the cardiac septa. (See pages 176, 177.)

1879 Henri-Louis Roger (1809–1891), of Paris, described the signs attending congenital defects of the interventricular septum. The characteristic murmur of this defect even today is known as the "bruit de Roger." (See page 187.)

1888 Étienne-Louis-Arthur Fallot (1850–1911), of Marseille, presented the most comprehensive account up to this time of "maladie bleue" (stenosis of the pulmonary artery, dextroposition of the aorta, defect of the interventricular septum and hypertrophy of the right ventricle). This combination of congenital anomalies has become known as the "tetralogy of Fallot." (See pages 195, 196.)

1897 Eisenmenger, of Germany, described an arrangement of congenital cardiac defects similar to that seen in the

tetralogy of Fallot. Instead of the pulmonary artery being narrowed, the pulmonary artery or valve is normal in size or dilated. This set of anomalies has since been known as "Eisenmenger's complex." (See page 207.)

1908 Maude E. Abbott (1869–1940), of Montreal, contributed extensively to the knowledge of congenital cardiac anomalies. It was largely through her data and teaching that the medical profession made rapid progress in the clinical recognition and identification of congenital defects of the heart and circulation. (See pages 237, 238.)

1911 Franklin Paine Mall (1862–1917), of Belle Plaine, Iowa, and Baltimore, applied his extensive knowledge of embryology in studying and demonstrating the scroll-like arrangement of the musculature of the ventricles. (See pages 244, 245.)

VI. THE CORONARY VESSELS AND THEIR DISEASES

1st century A.D.	Lucius Annaeus Seneca (4 B.C.–65 A.D.) presented a vivid description of his own symptoms of the disorder which, many centuries later, was named "angina pectoris." (See page 15.)
1669	Richard Lower (1631–1691), of Cornwall, demonstrated anastomoses between coronary arteries by experimentally injecting one artery from another. (See pages 61, 62.)
1679 and 1706	Théophile Bonet (Bonetus) (1620–1689), of Paris, described the case of an obese middle-aged poet who died within a few minutes following "distress in breathing." This may well have been sudden death due to coronary disease. (See pages 63, 64.)
1698	Pierre Chirac (1650–1732), of France, was apparently the first to investigate the effect of ligation of a coronary artery in the dog. He concluded that the procedure produced cardiac standstill. (See page 66.)
1703	Lorenzo Bellini (1643–1704), of Pisa, described calcification of the coronary arteries. (See page 64.)
1707 and 1728	Giovanni Maria Lancisi (1654–1720), of Rome, mentioned calcified coronary arteries as a cause of cardiac enlargement. He was aware of the disorder later to be known as "angina pectoris" and its relation to sudden death. Lancisi injected mercury into the coronary arteries of experimental animals and observed that it appeared in the chambers of the heart. He speculated that the mercury escaped through venous channels. (See pages 76, 77.)
1708	Adam Christianus Thebesius (1686–1732) injected materials into the coronary vessels and observed their passage into the chambers of the heart through small orifices in the endocardium. He also wrote about "ossification" of the coronary arteries. (See page 78.)
1710	Pierre Dionis (?–1718), of Paris, reported two cases of painful disorder of the thorax which he ascribed to disease of the heart and which may well have been examples of the anginal syndrome of coronary disease. (See page 78.)
1715	Raymond Vieussens (1641–1716), of Montpellier, described the course of the coronary arteries, the valve of the large coronary vein and the coronary sinus. He advanced the idea that the coronary vessels have direct communication with the chambers of the heart. (See pages 75, 76.)
1749	Jean-Baptiste de Sénac (1693–1770), of Versailles, described cases of coronary sclerosis in which painful seizures did not occur. He described marked thinning of the wall of the left ventricle (ventricular aneurysm) associated with coronary sclerosis. (See pages 81, 82.)
*1753**	Friedrich Hoffmann (1660–1742), of Halle, described the syndrome of angina pectoris without ascribing a name or a cause to the symptoms. (See pages 77, 78.)

* Posthumous publication.

1759°	The Earl of Clarendon (1609–1674), of London, gave one of the earliest published accounts of angina pectoris when he recorded the manner of death of his father. The account was written in 1632 but was not published until 1759. (See page 85.)
1761	John Baptist Morgagni (1682–1771), of Bologna, Padua and Venice, demonstrated sclerosis of the coronary arteries and called attention to patchy fibrous regions in the myocardium. He recorded rupture of the heart in instances of marked fatty myocardial changes which undoubtedly represented cardiac infarction. (See pages 85, 86.)
1768	Nicholas-François Rougnon de Magny, of France, recorded an instance of severe thoracic pain which terminated in sudden death of the patient. This may have been a case of coronary disease. (See page 87.)
1770°	Carolus Drelincourt (1633–1697), of France, described calcification of the coronary arteries, although he apparently did not appreciate the clinical significance of the findings. This observation was not published until seventy-three years after his death. (See page 74.)
18th century°	William Heberden (1710–1801), of London, described and named the clinical syndrome which has since become known as "angina pectoris" or, as he expressed it, "pectoris dolor." He believed the painful syndrome to be due to spasm of the heart. The work was not published until a year after Heberden's death. (See pages 87, 88.)
1776	John Fothergill (1712–1780), of Edinburgh and London, presented a case in which death occurred suddenly in a fit of anger. He made no comments relating to the attendant symptoms but expressed the belief that the patient was afflicted with the disease discussed by Heberden. In describing the postmortem findings (the postmortem was performed by John Hunter) he stated that the coronary arteries from their origins had "become one piece of bone." (See pages 89, 90.)
18th century	Robert Hamilton (1721–1793), of England, was probably the first to refer to the hereditary factors of angina pectoris. (See page 92.)
1798	John Abernethy (1764–1831), of London, confirmed the experiments of Vieussens and Thebesius. By making a "common coarse waxen injection" into the coronary arteries he observed that the wax flowed readily into the chambers of the heart. (See page 94.)
1799	Edward Jenner (1749–1823), of Berkeley, Gloucestershire, by careful observation at the bedside and at the postmortem table, related angina pectoris to obliterative arteriosclerosis of the coronary arteries. (See pages 94, 95.)
19th century	Jean-Nicolas Corvisart (1755–1821), of Paris, did not mention angina pectoris in his writings. He held the belief that coronary sclerosis limited the development of cardiac hypertrophy. (See pages 108, 109.)
1809	Allan Burns (1781–1813), of Glasgow, was an early exponent of the belief that angina pectoris occurs as the re-

° Posthumous publication.

sult of myocardial ischemia. He conducted the ligatured limb experiment to sustain his belief. Burns observed a thrombus in a coronary artery and commented on the flabby and fatty character of the heart. (See page 109.)

1812 John Warren (1753–1815), of Roxbury, Massachusetts, reported on four cases of angina pectoris, in one of which postmortem examination had been performed. In this case extensive pericardial adhesions were present and Warren concluded that "ossification" of the coronary arteries was not a prerequisite for the painful symptoms. (See pages 112, 113.)

1813 John Collins Warren (1778–1856), John Warren's son, also expressed skepticism regarding the relationship of diseases of the coronary arteries and angina pectoris. (See page 113.)

1814–1817 Friedrich Ludwig Kreysig (1770–1839), of Berlin, believed that spontaneous rupture of the heart was a relatively common event in spite of contradictory evidence. He described and discussed coronary sclerosis and commented on myocardial ischemia as the cause of angina pectoris. (See pages 113, 114.)

1815 Joseph Hodgson (1788–1869), of Birmingham, described a case of angina pectoris attended by sudden death in which postmortem examination revealed marked calcification of a main coronary artery and softening of the myocardium in the region supplied by this artery to such a degree that a finger could be thrust through the musculature. Hodgson had undoubtedly observed acute myocardial infarction with necrosis of tissue. (See page 114.)

1819 René-Théophile-Hyacinthe Laënnec (1781–1826), of Paris, considered angina pectoris a nervous affection of the heart. (See pages 115, 116.)

1827 Robert Adams (1791–1875), of Dublin, in the report of his case of heart block, commented on the extreme thinness of the left ventricle. Although he did not realize the implications of this observation, it may well have represented a region of healed or partially healed myocardial infarction. In another publication he discussed obliterative sclerosis of the coronary arteries. (See pages 116, 117.)

1829 Sir Dominic John Corrigan (1802–1880), of Dublin, believed that angina pectoris was a manifestation of aortitis. (See pages 122, 123.)

1830–1842 Jean Cruveilhier (1791–1873), of Paris, presented colored reproductions of myocardial infarcts but did not ascribe the changes noted to disease of the coronary arteries. He contended, however, that they did not represent fatty metamorphosis. (See pages 123, 124.)

1842 John E. Erichsen (1818–1896), of London, ligated the coronary arteries of dogs and rabbits and found that death of the animals occurred within ten minutes. He concluded from these experiments that any disease, such as "ossification" of the coronary arteries, that interferes with the flow of blood through them may result in sudden death. (See page 130.)

1845 John Forbes (1787–1861), of London, added more confusion to the prevailing bewilderment regarding the cause of angina pectoris. He contended that in approximately half of the cases of angina pectoris, no organic disease of the heart existed while in the other half a great variety of cardiac and especially aortic lesions occurred. (See page 133.)

1845–1846 Peter Mere Latham (1789–1875), of London, was the first to emphasize the sense of impending death which at times accompanies the anginal syndrome. Earlier, Latham had reported a group of cases in which sudden death did not occur in spite of the occurrence of severe seizures of angina pectoris and designated this condition as "pseudo-angina." (See page 134.)

1850 Sir Richard Quain (1816–1889), of London, described myocardial changes which correspond to our present-day concepts of anemic infarcts. He referred to them as "fatty degeneration." He stated that he had observed cases in which the myocardial changes were localized and corresponded to the region supplied by a coronary artery which was extensively "ossified." (See page 146.)

2nd half of the 19th century Rudolph Ludwig Karl Virchow (1821–1902), of Berlin, failed to recognize the true significance of the myofibrosis of chronic myocardial ischemia and designated the fibrous changes as chronic myocarditis. (See pages 151, 152, 153.)

1861 Pehr Henrik Malmsten (1811–1883), of Sweden, reported a case of spontaneous rupture of the left ventricle and definitely related coronary thrombosis to cardiac infarction and rupture. (See page 154.)

1862 Peter Ludwig Panum (1820–1885), of Kiel and Copenhagen, confirmed Erichsen's experiments but instead of ligating the coronary arteries he utilized the method of experimental emboli. While death of the animals occurred, the cessation of cardiac action was gradual rather than abrupt. (See page 157.)

1864 Étienne Lancereaux (1829–1910), of Paris, reported the finding of lesions in the cardiac plexus and advanced the belief that neuritis of these tissues was responsible for angina pectoris. (See pages 158, 159.)

1867 Sir Thomas Lauder Brunton (1844–1916), of Edinburgh and London, ascribed angina pectoris specifically to vascular spasm of the vessels of the heart. (See page 159.)

1867 Hermann Nothnagel (1841–1905), of Freiburg, Jena and Vienna, introduced a hypothesis regarding the cause of angina pectoris, which condition he designated as "stenocardia." He contended that the painful seizures did not arise from primary disease of the heart but rather from secondary factors comprising generalized arterial spasm. (See page 161.)

1873 Josef Hyrtl (1810–1894), of Vienna, studied the vascularity of the heart and other organs by employing the injection-corrosion method. He contended that anastomoses between coronary arteries did not exist. (See page 150.)

1874 Charles Hilton Fagge (1838–1883), of Hythe and London, described myocardial changes which unquestionably represented infarcts but he did not recognize their true nature. He described regions of patchy myofibrosis, the thinning of the ventricular wall and the occurrence of ventricular aneurysm. No mention was made of the coronary arteries. (See pages 174, 175.)

1877 Sir William T. Gairdner (1824–1907), of London, was the first to call attention to the painless form of angina pectoris which he designated as "angina pectoris sine dolore." (See page 181.)

1878 Adam Hammer (1818–1878), of St. Louis, Missouri, and Vienna, was the first to diagnose coronary thrombosis correctly during the life of the patient. (See page 182.)

1880 Carl Weigert (1845–1904), of Münsterberg, Silesia, was the first exponent of the doctrine of cardiac infarction. His description of infarcts was clear and concise and he fully realized the relationship of the myocardial changes to obliterative changes in the coronary arteries. Weigert's account is classic. (See page 189.)

1880 Frederick Winsor (1829–1889), of Massachusetts, described a case of angina pectoris with spontaneous rupture of the heart and clearly portrayed coronary occlusion, myocardial infarction and rupture. (See pages 189, 190.)

1881 Julius Friedrich Cohnheim (1839–1884), of Kiel and Berlin, in collaboration with von Schulthess-Rechberg, conducted experiments with reference to the coronary arteries. The coronary arteries of curarized dogs were obstructed by the application of clamps and the authors concluded that the mechanical obstruction of either main coronary artery caused the ventricles to become arrested in diastole within a period of two minutes. This led them to accept the belief that the coronary arteries were end arteries and that if any anastomoses existed they must exist in the form of minute capillaries. Cohnheim also described sudden death from coronary embolism. (See pages 179, 180, 181.)

1884 Ernst von Leyden (1832–1910), of Danzig and Berlin, described four forms of coronary disease: (1) sclerosis of the coronary arteries without symptoms of cardiac impairment, (2) thrombotic obstruction of a coronary artery with acute softening and hemorrhagic infarction of the myocardium, (3) a chronic type of coronary obliteration resulting in patchy or diffuse fibrosis of the myocardium, with weakening of the ventricular wall, at times eventuating in formation of cardiac aneurysm and (4) a mixed form of chronic fibrosis associated with acute infarction of the myocardium. (See page 192.)

1887 Ernst Ziegler (1849–1905), of Freiburg, presented the most classic description of cardiac infarction up to this time. (See pages 192, 193.)

1889 Henri Huchard (1844–1910), of Auxon (Aube), discussed the variable clinical phenomena of coronary disease and considered spasm of the coronary arteries to be one of a number of causes of angina pectoris. (See page 197.)

1892 Ludwig Hektoen (1863–), of Chicago, recorded one of the first articles dealing with the medicolegal aspects of sudden death with special reference to coronary disease. (See pages 199, 200.)

1894 William Townsend Porter (1862–), of Cambridge, Massachusetts, conducted experiments on ligation of the coronary arteries. He noted that the procedure frequently resulted in fibrillary contractions of the heart and sudden death. However, death did not always occur and this led him to conclude that Cohnheim's (1881) consistently fatal resulted in fibrillary contractions of the heart and sudden arteries were not end arteries. (See page 203.)

1896 George Dock (1860–), of Galveston, Ann Arbor, New Orleans and St. Louis, recorded the first case of coronary thrombosis diagnosed in the United States during the life of the patient. (See page 203.)

1896 René Marie (1868–), of Paris, contended that, when a coronary artery of considerable size becomes occluded by a thrombus (not by an embolus), infarction of the myocardium results. The artery which becomes occluded is usually sclerotic. Marie described the various changes occurring in the myocardium during infarction. (See pag 204.)

1896 Sir William Osler (1849–1919), of Canada, the United States and England, discussed the hereditary factors of angina pectoris. (See pages 239, 240.)

1898 George Alexander Gibson (1854–1913), of Edinburgh, published a splendid work on diseases of the heart and aorta. His comments regarding angina pectoris clearly indicated the uncertainty and confusion which prevailed regarding the coronary arteries and their diseases as the nineteenth century came to a close. (See page 209.)

1899 Walter Baumgartner, working in Porter's laboratory, repeated Porter's experiments and produced infarcts of the myocardium. (See page 203.)

1908–1914 Sir James Mackenzie (1853–1925), of Burnley and London, accepted and advocated the ischemic origin of angina pectoris in its relation to obliterative disease of the coronary arteries. (See pages 233, 234.)

1912 James Bryan Herrick (1861–), of Chicago, recorded the first truly representative and influential account regarding the clinical recognition of coronary thrombosis. In 1919 he reported a case of coronary thrombosis which was studied by means of electrocardiographic records. (See page 245.)

1915 Sir Thomas Clifford Allbutt (1836–1925), of Cambridge, held the belief that angina pectoris was due to disease of the root of the aorta. (See pages 248, 249, 250.)

1920 Harold Ensign Bennett Pardee (1886–), of New York, presented the first detailed description of the changes in the T waves of the electrocardiogram occurring in sudden obstruction of the coronary arteries. (See pages 255, 256.)

1921 Louis-Henri Vaquez (1860–1936), of Paris, contended that angina pectoris was an expression of irritation of the cardio-aortic plexus. (See page 256.)

VII. ELECTROPHYSIOLOGY AND ELECTROCARDIOGRAPHY

18th century	Luigi Galvani (1737–1798), of Bologna, investigated animal electricity. One day while working in his laboratory, Galvani had placed a dissected frog on a table near an electric machine. When his assistant touched the nerves of the frog's leg with a knife, the leg contracted vigorously. Galvani investigated this peculiar phenomenon and finally discovered that the leg would contract when the nerve was touched only if the electric machine was sparking. (See pages 72, 132.)
18th and 19th centuries	Johannes S. C. Schweigger (1779–1857), of the University of Halle, invented the string galvanometer. (See pages 133, 228, 338.)
1843	Carlo Matteucci (1811–1868), of Forlì, placed the central end of the severed peripheral segment of the sciatic nerve of one leg of a frog on the muscles of the opposite leg. When the sciatic nerve on the intact side was stimulated, the muscles of both legs contracted, although only the intact side had been stimulated. (See pages 132, 133.)
1855	Albert von Kölliker (1817–1905), of Zurich and Würzburg, conducted an important experiment in electrophysiology which virtually established the basis of electrocardiography. He applied Matteucci's galvanic frog experiment to the heart and demonstrated that with each beat of the frog's heart a definite electric current was produced. This work established the occurrence of action currents resulting from cardiac activity. This experimental work was conducted in collaboration with H. Müller. (See page 153.)
1865	Carl Ludwig (1816–1895), of Marburg, Zurich and Leipzig, showed that the normal beat of the animal heart is abolished by the application of faradic stimulation. (See page 136.)
1880	Sir John Burdon Sanderson (1828–1905), of England, in collaboration with F. J. M. Page, was the first to record the electrical activity of the heart by means of the capillary electrometer. (See pages 186, 187.)
2nd half of the 19th century	Henry Pickering Bowditch (1840–1911), of Boston, conducted important experiments with reference to the physiology of the heart muscle. By direct electrical stimulation of the myocardium with uniform intensity and frequency, he found that the first few contractions increased with remarkable regularity. This gradual increase in the extent of muscular shortening with a constant stimulus led Bowditch to name this behavior "treppe" or staircase phenomenon. After this period had been passed, the contractions were found to diminish steadily until muscular fatigue ensued and no further response to stimulation occurred. (See page 167.)
1887	John Alexander MacWilliam (1857–1937), of Aberdeen and London, conducted experiments in which he produced

fibrillation of the heart by electrical means. He showed that fibrillation results from "a rapid succession of incoordinated peristaltic contractions," described the relationship of the refractory period to these changes and presented evidence to the effect that certain poisons, when injected into the blood stream, result in fibrillation of the ventricles. (See pages 194, 195.)

1903 Willem Einthoven (1860–1927), of Leyden, adapted the string galvanometer for recording the action currents of the heart. His demonstration established the science of electrocardiography. Einthoven made many important contributions to this new field. (See pages 228, 229.)

1910 Sir Thomas Lewis (1881–1945), of London, proved by means of electrocardiography that the cardiac impulse has its origin in the sino-auricular node (node of Keith and Flack). (See pages 241, 242.)

VIII. THE ENDOCARDIUM AND ITS DISEASES

Circa 1630	Fabrizio Bartoletti, of Italy, described ulceration of the heart (ulcerative endocarditis) and "ossification" of the aortic valve. (See pages 56, 57.)
1646	Lazare Riviere (Riverius) (1589–1655), of Montpellier, was apparently the first to describe stenosis of the aortic valve. (See page 58.)
1674	John Mayow (1643–1679), of Cornwall, described dilatation of the left auricle and right ventricle in stenosis of the mitral valve. (See pages 62, 63.)
1679 and 1706	Théophile Bonet (Bonetus), (1620–1689), of Paris, recorded an instance of sudden death in which postmortem examination revealed calcareous stenosis of the aortic valve. (See pages 63, 64.)
1707	William Cowper (1666–1709), of London, described aortic insufficiency and recorded an example of stenosis of the aortic valve. (See pages 74, 75.)
1715	Raymond Vieussens (1641–1716), of Montpellier, discussed the back pressure phenomena in mitral stenosis and described the resulting symptoms. In 1695 while discussing aortic insufficiency, he had commented on the peculiar water-hammer pulse attending this valvular defect. Vieussens had described mitral stenosis and its pathologic features in 1705. (See pages 75, 76.)
1749	Jean-Baptiste de Sénac (1693–1770), of Versailles, described an instance in which a murmur was so loud that it could be heard some distance from the patient. (See pages 81, 82.)
1761	John Baptist Morgagni (1682–1771), of Bologna, Padua and Venice, described lesions of the aortic, mitral, pulmonary and tricuspid valves and presented instances of mitral stenosis, calcareous stenosis of the aortic valve and aortic regurgitation. (See pages 85, 86.)
1788	Matthew Baillie (1761–1823), of London, mentioned rheumatism of the heart. (See pages 92, 93.)
1788	David Pitcairn (1711–1791), of London, discussed "rheumatism of the heart" but this work was never published. (See page 93.)
1789	Edward Jenner (1749–1823), of Berkeley, Gloucestershire, delivered "Remarks on a disease of the heart following acute rheumatism." This oration was never published and become lost and is historically known as the "Lost manuscript." (See pages 94, 95.)
19th century	Jean-Nicolas Corvisart (1755–1821), of Paris, separated heart failure into three stages and discussed the relationship of valvular lesions to the development of heart failure. He was the first to mention and interpret thrills over the precordium in the diagnosis of cardiac disease, particularly in mitral stenosis. Corvisart described the clinical symptoms and postmortem findings in tricuspid steno-

sis and discussed myocarditis and its frequent association with endocarditis and pericarditis. He was the first to evolve the concept of pancarditis. (See pages 108, 109.)

1809 — Allan Burns (1781–1813), of Glasgow, described the symptoms and the pathologic findings in combined mitral and aortic disease. (See pages 109, 110, 111.)

1810 and 1812 — William Charles Wells (1757–1817), of Charleston, South Carolina, and England, described the symptoms of "rheumatism of the heart" and stressed oppression in the thorax, dyspnea, the occasional occurrence of hemoptysis and palpitation and tachycardia. (See page 112.)

1824 — René-Joseph-Hyacinthe Bertin (1767–1828), of Paris, described valvular vegetations and valvular deformities with special reference to their signs and described the presystolic murmur of mitral stenosis. (See page 124.)

1828–1829 — Thomas Hodgkin (1798–1866), of Tottenham and London, presented an excellent account of insufficiency of the aortic valve, called attention to the to-and-fro murmurs and commented on the full bounding pulse. (See pages 117, 118.)

Circa 1830 — Robert Adams (1791–1875), of Dublin, discussed mitral and aortic stenosis. He held the belief that the valves of the left side of the heart were more subject to disease than those of the right side because their closure was more perfect. (See pages 116, 117.)

1831 — James Hope (1801–1841), of Edinburgh and London, described the physical signs of aortic, mitral and pulmonary valvular stenosis and aortic insufficiency. He also postulated the signs that should attend stenosis of the tricuspid valve and described the systolic murmur of mitral insufficiency. (See pages 121, 122.)

1832 — Sir Dominic John Corrigan (1802–1880), of Dublin, discussed the origin of the diastolic murmur and clearly described and discussed the characteristic bounding or "water-hammer" pulse of aortic insufficiency, which even today is frequently referred to as the "Corrigan pulse." A year later he criticized Laënnec's interpretation of the physical phenomena designated by the latter as "bruit de soufflet" and "frémissement cataire." Corrigan contended that they were not the result of spasm but resulted from organic valvular changes. (See pages 122, 123.)

1835 — Jean-Baptiste Bouillaud (1796–1881), of Angoulême and Paris, gave the most classic account of endocarditis up to this time. He divided endocarditis into three stages: (1) that of "sanguinary congestion, of softening and of ulceration or suppuration" (acute endocarditis); (2) that of "organization of secreted products or of a portion of fibrinous concretions" (subacute endocarditis) and (3) that of "cartilaginous, osseous or calcareous induration of the endocardium in general and of the valves in particular, with or without narrowing of the orifices of the heart" (chronic or healed endocarditis). In 1836 he irrevocably established the etiologic relationship between rheumatic fever and heart disease. (See pages 124, 125, 126.)

1836	Charles J. B. Williams (1805–1889), of England, gave the first complete description of the murmurs of mitral stenosis and emphasized the diastolic murmur. (See pages 126, 127.)
1842	Norman Chevers (1818–1886), of London, expressed the opinion that the signs accompanying stenosis of the aortic valve could appear in the absence of aortic disease. He observed vegetations situated on the interventricular septum near the attachment of the aortic cusp of the mitral valve which gave rise to signs simulating the aforementioned valvular defect. (See pages 130, 131.)
1843	Sulpice-Antoine Fauvel (1813–1884), of Paris and Constantinople, recorded an accurate account of the signs of mitral stenosis. (See pages 131, 132.)
1st half of the 19th century	William Stokes (1804–1878), of Dublin, contrary to prevailing opinion, correctly contended that the prognosis in mitral valvular disease was more serious than in aortic lesions. (See pages 134, 135.)
1852	William Senhouse Kirkes (1823–1864), of London, recorded one of the earliest and most concise accounts of the disease now known as "bacterial endocarditis." (See pages 148, 149.)
1846–1856	Rudolph Ludwig Karl Virchow (1821–1902), of Berlin, demonstrated the embolic nature of the pulmonary lesions in bacterial (malignant) endocarditis. (See pages 151-153.)
1861	Paul-Louis Duroziez (1826–1897), of Paris, described the double murmur heard in the femoral artery in aortic insufficiency which still today is known as "Duroziez' sign." He also described the pure form of mitral stenosis and called attention to certain sequelae of this lesion such as embolism, aphasia and hemiplegia. Duroziez noted the predominance of mitral disease among women. (See pages 154, 155.)
1862	Austin Flint (1812–1886), of Petersham, Massachusetts, Buffalo and Louisville, was one of the first to use the binaural stethoscope. He reported a case in which examination revealed the typical signs of aortic insufficiency and stenosis but in addition to these signs, a presystolic murmur was audible at the apex of the heart. However, at postmortem examination, the mitral valves were found to be normal. Since that time, the murmur described by Flint has been known by his name. (See pages 155, 156, 157.)
1864	Étienne Lancereaux (1829–1910), of Paris, discussed chronic myocarditis and stated that it occurred from toxic causes as well as being associated with endocarditis and pericarditis. (See pages 158, 159.)
2nd half of the 19th century	Hermann Nothnagel (1841–1905), of Freiburg, Jena and Vienna, ascribed pain to valvular lesions and reported on the relative frequency of this symptom according to the valve or valves involved. (See page 161.)
2nd half of the 19th century	Pierre-Carl-Edouard Potain (1825–1901), of Paris, made precise studies on the relationship of tricuspid insufficiency and the attending circulatory disturbances, described the

	pulsations of the liver occurring with this valvular defect and explained the mechanism of the apex beat. (See pages 161, 162, 163.)
1868	Heinrich Irenaeus Quincke (1842–1922), of Berlin and Kiel, was the first to make detailed studies of the capillary pulse and to note its significance in the diagnosis of aortic insufficiency. (See pages 163, 164.)
1870	E. F. H. Winge (1827–1894), of Christiania (Oslo), described the form of endocarditis now known as "acute bacterial endocarditis." (See pages 164, 165.)
1870	Sir Samuel Wilks (1824–1911), of London, gave a splendid account of bacterial endocarditis. (See pages 165, 166.)
1872	Hjalmar Heiberg (1837–1897), of Christiania (Oslo), recorded a case of acute bacterial endocarditis complicating puerperal sepsis. (See pages 170, 171.)
2nd half of the 19th century	Carl Rokitansky (1804–1878), of Vienna, was the first actually to demonstrate the presence of micro-organisms in the vegetations of acute endocarditis. (See pages 176, 177.)
2nd half of the 19th century	Ernst von Leyden (1832–1910), of Danzig and Berlin, described instances of recurrent febrile episodes in patients with healed valvular lesions, which undoubtedly were instances of what is now known as "subacute bacterial endocarditis." (See page 192.)
1888	Graham Steell (1851–1942), of Manchester, described the diastolic murmur of pulmonary regurgitation which at times accompanies the increased intrapulmonary pressure associated with mitral stenosis. This murmur is still known as the "Graham Steell murmur." (See page 195.)
1903	Hermann Lenhartz (1854–1910), of Germany, described the various forms of endocarditis, including their symptomatology and bacteriologic features. He described the features of a form of endocarditis which he insisted differed from the acute ulcerative type (acute bacterial endocarditis) and related it to the organism which he designated as "Streptococcus parvus" (streptococcus viridans). (See page 230.)
1905	William Sydney Thayer (1864–1932) of Milton, Massachusetts, and Baltimore, discussed gonorrheal septicemia and endocarditis. At a later date he was the first to call attention to the fact that gonorrheal endocarditis at times runs a subacute course. (See pages 235, 236.)
1909	Sir William Osler (1849–1919), of Canada, the United States and England, gave a splendid account of the disease now known as "subacute bacterial endocarditis" and described the evanescent painful embolic subcutaneous nodules (pathognomonic of the disease) since known as "Osler's nodes." (See pages 239, 240.)
1909	Edward Carl Rosenow (1875–), of Chicago and Rochester, Minnesota, conducted pioneer experiments on the production of endocarditis in animals using both pneumococci and staphylococci. The micro-organisms which he believed were pneumococci were ultimately shown to be streptococci. (See pages 240, 241.)

1910 Emanuel Libman (1872–1946), of New York, in collaboration with H. L. Celler, published his important article on "subacute infective endocarditis" (subacute bacterial endocarditis). He accurately described the clinical features and the course of the disease and discussed the cultural characteristics of the recovered streptococci in detail. In 1913 Libman described the clinical and pathologic features of the bacteria-free stage of subacute bacterial endocarditis. In 1924, in collaboration with Benjamin Sacks, Libman published his important article on "Atypical verrucous endocarditis" (Libman-Sacks disease.) (See pages 242, 243.)

1910 Hugo Schottmüller (1867–1929), of Germany, reported his experience with the so-called chronic cases, which he termed "endocarditis lenta" (subacute bacterial endocarditis). He had uniformly isolated a micro-organism which he believed merited a separate classification owing to its remarkably characteristic cultural behavior. Schottmüller called it "Streptococcus viridans." (See pages 243, 244.)

IX. HEART BLOCK

*1719**	Marcus Gerbezius (Verbez) (?–1718) observed and described two cases of extremely slow pulse associated with convulsive syncope which undoubtedly represented instances of complete heart block. The publication appeared a year after his death. (See page 79.)
1761	John Baptist Morgagni (1682–1771), of Bologna, Padua and Venice, described heart block. (See pages 85, 86.)
1793	Thomas Spens (1769–1842), of Edinburgh, described a case of remarkable slowness of the pulse (twenty-four beats each minute) in which death occurred suddenly after several episodes of unconsciousness. (See page 93.)
1827	Sir William Burnett (1779–1861), of Montrose, Edinburgh and Chichester, reported a case of complete heart block with convulsive syncope. (See page 116.)
1827	Robert Adams (1791–1875), of Dublin, described heart block associated with convulsive syncope in a patient whose heart showed marked infiltration with fat. The cerebral symptoms described later became known as "Adams-Stokes syndrome." (See pages 116, 117.)
1846	William Stokes (1804–1878), of Dublin, especially emphasized the convulsive seizures frequently accompanying heart block. Even today, the convulsive syncopal attacks of complete heart block are known as "Adams-Stokes seizures." (See pages 134, 135.)
1852	Hermann Stannius (1808–1883), of Hamburg, applied a ligature at the junction of the auricle and the sinus venosus of the frog's heart which resulted in standstill of the heart. The application of a second ligature to the auriculoventricular groove caused the ventricles to beat again. In this experiment, Stannius demonstrated the important fact that the ventricles are endowed with the property of initiating their own rhythm in heart block (idioventricular rhythm). (See page 149.)
1885–1886	Walter Holbrook Gaskell (1847–1914), of Cambridge, produced experimental heart block in animals. (See page 191.)
1889	Henri Huchard (1844–1910), of Auxon (Aube), investigated heart block and suggested that it might be the result of arteriosclerosis of the cerebral arteries, particularly those of the medulla. He suggested that heart block be called "Adams-Stokes disease." (See page 197.)

* Posthumous publication.

X. MILESTONES IN MEDICAL EDUCATION

3000–2500 B.C.	Imhotep (?) of ancient Egypt (Edwin Smith Surgical Papyrus, discovered in 1862), gave detailed instructions (presumably to other physicians, healers or priests) as to the method to be employed in examining a patient. (See pages 6, 7.)
6th century B.C. and later	The early Greek philosophers speculated and investigated the workings of the human mind, considered commonplace and abstract subjects and taught by conversation and discussion. These educational principles pervaded medicine. (See pages 10–14.)
5th and 4th centuries B.C.	Hippocrates (460–370 B.C.) of Cos advocated mental concentration and analysis together with the utilization of the five senses. His doctrines and aphorisms formed the text for many generations of physicians. (See pages 11, 12.)
After 322 B.C.	School of Alexandria: Erasistratus, father of physiology; Herophilus, dissected human bodies in public, father of anatomy. (See pages 13, 14.)
2nd and 3rd centuries A.D.	Claudius Galen (138–201 A.D.) of Pergamon erroneously conceived the anatomy and physiology of the cardiovascular system. However, his teaching was so forceful that his errors were perpetuated for approximately fourteen centuries. (See pages 16–19.)
9th century	Founding of the famous school of Salerno. (See page 26.)
10th and 11th centuries	Avicenna (980–1037), a Persian physician, retarded medical education when he advocated deductive and speculative reasoning as superior to direct observation. (See page 28.)
*1507**	Antonio Benivieni (circa 1440–1502), of Florence, is credited with being the founder of pathology before Morgagni. (See page 33.)
15th and 16th centuries	Leonardo da Vinci (1452–1519), the Italian genius of many talents, a great artist, was the originator of modern medical illustration. The graphic method of medical illustration has played an important role in medical education. (See pages 33–36.)
17th century	Founding of the Royal Society of London. (See pages 52–54.)
17th century	Lazare Riviere (Riverius) (1589–1655), of Montpellier, was greatly interested in the drug therapy of diseases and introduced the teaching of chemistry into the curriculum of the Montpellier School. (See page 58.)
17th century	Jean Pecquet (1622–1674), of Dieppe, was one of the early teachers of Harvey's doctrines regarding the heart and circulation. (See page 58.)
17th century	The Dutch School of anatomists flourished under the brilliant teaching of Pieter Paaw, Nicholas Tulp, Sebastian Egbert de Vriz and Regnier de Graaf. (See pages 58, 59.)

* Posthumous publication.

17th century	Marcello Malpighi (1628–1694), of Bologna, Pisa and Messina, was the founder of histology. (See page 59.)
17th century	Giovanni Guglielmo Riva (1627–1677), of Asti, founded a society of pathologists and originated an anatomic museum. (See page 62.)
1674	John Mayow (1643–1679), of Cornwall, was one of the pioneer physiologists. (See pages 62, 63.)
17th century	Antony van Leeuwenhoek (1632–1723), of Delft, furthered the science of microscopy and ground more than 400 lenses. (See pages 64, 65.)
18th century	Giorgio Baglivi (1668–1706), of Rome, was a pioneer exponent of bedside medical instruction and stressed the principles of reasoning and observation. He also advocated specialization in medical practice. To his students, Baglivi stressed the philosophy that the best book of medical knowledge is the recitation of the patient's symptoms. (See pages 72, 73.)
1726	Francesco Ippolito Albertini (1662–1738), of Bologna, advocated the correlation of symptoms of disease with pathologic findings. He taught the importance of inspection and palpation. (See pages 73, 74.)
18th century	Hermann Boerhaave (1668–1738), of Leyden, was a great teacher and a founder of the Eclectic School of Medicine. He was a Hippocratist in principle. (See pages 79, 80.)
18th century	John Baptist Morgagni (1682–1771), of Bologna, Padua and Venice, was the true founder of systematic pathologic anatomy. (See pages 85, 86.)
19th century	Jean-Nicolas Corvisart (1755–1821), of Paris, the brilliant teacher and clinician, was an ardent advocate of postmortem examination. His teaching stressed the importance of proving the correctness or error of clinical diagnosis. (See pages 108, 109.)
1819	René-Théophile-Hyacinthe Laënnec (1781–1826), of Paris, by his invention of the stethoscope and the development of auscultation completely revolutionized the study and teaching of diseases of the heart and lungs. (See pages 115, 116.)
19th century	Richard Bright (1789–1858), of London, an inspiring teacher, was an accomplished artist and used this talent both in teaching and in the illustration of some of his writings. (See page 127.)
19th century	Joseph Skoda (1805–1881), of Pilsen and Vienna, was one of the greatest teachers of the Viennese school. A master clinician, he acquired amazing precision in the utilization of physical diagnosis. (See page 128.)
Circa 1845	Carl Ludwig (1816–1895), [illegible] and Leipzig, introduced the graphic [illegible] investigation by the use of such apparatus as the kymograph, blood pump and Stromuhr. He was a pioneer in perfusion experiments on excised organs. (See page 136.)
2nd half of the 19th century	Claude Bernard (1813–1878), of Paris, the great physiologist, was the founder of experimental medicine. (See pages 147, 148.)

2nd half of the 19th century	Jacob Mendes DaCosta (1833–1900), of Philadelphia, did much to instill vigor and imagination into American medical teaching. At this time teaching consisted of literally memorizing a textbook and being able to pass examinations. Actual bedside instruction was not emphasized until DaCosta set the pattern in his brilliant method of teaching. (See page 168.)
2nd half of the 19th century	Ludwig Traube (1818–1876), of Berlin, was one of the founders of experimental pathology. (See pages 168–170.)
1896	Sir William Osler (1849–1919), of Canada, the United States and England, together with William Welch, W. S. Halsted, Henry M. Hurd and Howard A. Kelly, inaugurated a new and brilliant era of medical education in America. (See pages 239, 240.)
1911–1914	Richard Clarke Cabot (1868–1939), of Boston, introduced a more precise and uniform classification of diseases of the heart. His case method of teaching was a great step forward. (See pages 247, 248.)
1919	Sir James Mackenzie (1853–1925), of Burnley and London, decried the rules of certain outstanding medical organizations which excluded capable clinicians from membership because they had not participated in laboratory research. (See pages 233, 234.)
1st quarter of the 20th century	Sir Thomas Clifford Allbutt (1836–1925), of Cambridge, in addition to being a great clinician was an able teacher. He was a gifted writer and few medical authors have ever equalled his eloquent diction. Allbutt made numerous contributions dealing with the history of medicine. (See pages 248, 249, 250.)
1st quarter of the 20th century	Karel Frederik Wenckebach (1864–1940), of Groningen and Vienna, was a celebrated teacher. He emphasized practical methods of teaching, yet stressed the accessory importance of instruments of precision. Wenckebach attracted graduate students from all quarters of the world. (See pages 229, 230.)
1st quarter of the 20th century	Franklin Paine Mall (1862–1917), of Belle Plaine, Iowa, and Baltimore, was one of America's outstanding teachers of anatomy and embryology. (See pages 244, 245.)

XI. PAROXYSMAL TACHYCARDIA

1835	Charles J. B. Williams (1805–1889), of England, described paroxysmal tachycardia. (See pages 126, 127.)
Circa 1850	William Stokes (1804–1878), of Dublin, recognized and described paroxysmal tachycardia. (See pages 134, 135.)
1867	Richard Payne Cotton (1820–1877), of London, reported a case of paroxysmal tachycardia in which the rate of the heart was 232 beats per minute. (See pages 160, 161.)
2nd half of the 19th century	Hermann Nothnagel (1841–1905), of Freiburg, Jena and Vienna, suggested that paroxysmal tachycardia resulted from irritation of the sympathetic nervous system. (See page 161.)
1888	John S. Bristowe (1827–1893), of London, wrote an able account of paroxysmal tachycardia. He commented on the intermittent character of the disorder, its relative frequency, its sudden onset and abrupt termination, and its occurrence in patients with apparently normal hearts. (See pages 196, 197.)
1889	Leon Bouveret (1850–1929), of Lyon, named the paroxysmal seizures of rapid cardiac acceleration, *tachycardie essentielle paroxystique* (essential paroxysmal tachycardia). (See page 197.)

XII. PATHOLOGY OF THE HEART AND CIRCULATION

5th and 4th centuries B.C.	Hippocrates (460–370 B.C.) of Cos held the belief that the heart was not susceptible to disease because of its compact structure. (See pages 11, 12.)
4th and 3rd centuries B.C.	Erasistratus (310–250 B.C.) of Alexandria is believed to have been the first to display interest in pathologic anatomy when he searched for evidence relative to the causes of pleuritis and pericarditis. His basic concept regarding diseases was that of plethora (hyperemia). He considered plethora to be the cause of angina (sore throat), pleuritis and dropsy. (See pages 13, 14.)
1st century A.D.	Aurelius (Aulus) Cornelius Celsus, early Roman encyclopedist, was the first to write in Latin about disease of the heart. He discussed the mysterious disease vaguely denoted by the ancients as "kardiakon." Celsus insisted that it represented only a marked weakness of the body resulting from profuse sweating and that it was associated with slow and weak pulsations of the arteries. (See pages 14, 15.)
2nd and 3rd centuries	Claudius Galen (138–201 A.D.) of Pergamon described a tumor of the pericardium in a monkey. He also discussed wounds of the heart and emphasized the fact that penetrating wounds of a heart chamber were the most serious, especially those of the left side of the heart. (See pages 16, 17, 18, 19.)
9th and 10th centuries	Rhazes (865–925), an ancient Persian physician, discussed the importance of the state of the heart in infectious diseases. (See page 20.)
12th century	Avenzoar (1113–1162), of Cordoba, Spain, and Arabia, discussed diseases of the heart and distinguished between primary disease and sympathetic (nervous) disorders. (See page 28.)
*1507**	Antonio Benivieni (circa 1440–1502), of Florence, wrote an extensive work on morbid anatomy which was published five years after his death. He observed postmortem thrombi in the chambers of the heart which he erroneously interpreted as being polypi. Benivieni reported on twenty postmortem examinations and is credited with being the founder of pathology before Morgagni. (See page 33.)
1521	Jacopo Berengario da Carpi (1470–1550), of Bologna and Ferrara, mentioned dilatation of the heart. (See page 36.)
16th century	Paracelsus (1493–1541), of Einsiedeln, Switzerland, compared apoplexy to a stroke of lightning. (See page 36.)
Circa 1534	Nicolo Messa (?–1569), of Padua, described cardiac hypertrophy when he wrote about a swelling involving both sides of the heart which resulted in great enlargement of the organ. (See page 38.)
1551	Andreas Vesalius (1514–1564), of Padua, was the first to recognize and describe aneurysm of the thoracic and abdominal aorta. (See pages 38, 39.)

* Posthumous publication.

Circa 1630	Fabrizio Bartoletti, of Italy, described pericardial adhesions, fatty accumulations in the pericardium, ulceration of the heart (ulcerative endocarditis) and "ossification" of the aortic valves. He also discussed intracardiac thrombi and believed them to be cardiac polypi. (See pages 56, 57.)
17th century	Nicholas Tulp (Tulpius) (1593–1674), of Amsterdam, described true polyps of the heart and distinguished them from postmortem thrombi. (See pages 58, 59.)
1658	Johann Jacob Wepfer (1620–1695), of Schaffhausen, was the first to establish definitely the causative relationship between cerebral hemorrhage and apoplexy. (See page 59.)
1660°	William Harvey (1578–1657), of Folkestone and London, recorded the first instance of spontaneous rupture of the left ventricle. (See pages 54, 55, 56.)
1670	Theodor Kerckring (1640–1693), of Amsterdam, recognized postmortem thrombi within the chambers of the heart and stated that they were neither polyps nor worms. (See page 62.)
Circa 1700	Giorgio Baglivi (1668–1706), of Rome, recorded classic descriptions of cardiac failure, cardiac asthma, arteriosclerosis of the cerebral arteries and calcification of the pericardium. (See pages 72, 73.)
1707	Giovanni Maria Lancisi (1654–1720), of Rome, correlated postmortem findings with clinical symptoms and signs. He investigated the causes of sudden death and found that cardiac enlargement played an important role. He mentioned calcified coronary arteries as a cause of cardiac enlargement. Lancisi was aware of the disorder later to be known as "angina pectoris" and its relation to sudden death. Lancisi differentiated cardiac hypertrophy from dilatation and described valvular vegetations and calcification of the cardiac valves. He emphasized the role of the mechanical barriers of both arterial and valvular disease in the production of cardiac enlargement. Lancisi was the first to describe syphilis of the heart. He appears to have been the first to mention the hereditary tendency to cardiac disease when he stated that the tendencies are transmitted from parent to child. (See pages 76, 77.)
1726	Francesco Ippolito Albertini (1662–1738), of Bologna, recognized that the enlarged heart was a diseased heart. He described pulmonary edema and stated that it was the result of impaired circulation in and through the heart. Albertini ascribed dyspnea to congestion of the lungs and stated that its progression eventuated in hydrothorax. He differentiated pulmonary congestion and pulmonary edema from hydrothorax. (See pages 73, 74.)
1728	Hermann Boerhaave (1668–1738), of Leyden, described the case of a patient who died from suffocation resulting from a huge fatty mediastinal tumor. Boerhaave found the heart to be tremendously enlarged. (See pages 79, 80.)

° Posthumous publication.

1749 Jean-Baptiste de Sénac (1693–1770), of Versailles, recorded observations indicating that the incidence of heart disease increased with age and he investigated the amount of epicardial fat present according to age periods. He made attempts to evaluate the degree of danger attending wounds in various portions of the heart. Sénac investigated the mode of production of cardiac dilatation. He noted and commented on atrophy of the heart and emphasized the fact that all the structures of the heart were susceptible to inflammatory diseases. (See pages 81, 82.)

1761 John Baptist Morgagni (1682–1771), of Bologna, Padua and Venice, described lesions of the aortic, mitral, pulmonary and tricuspid valves and presented instances of mitral stenosis, calcareous stenosis of the aortic valve and aortic regurgitation. He demonstrated coronary sclerosis and aneurysm of the aorta. Morgagni ascribed the fibrous changes in the myocardium to degenerative rather than to inflammatory disease. He also recorded instances of spontaneous rupture of the heart. (See pages 85, 86.)

1761 Frank Nicholls reported the postmortem findings in the case of George II, who died suddenly. Evidence according to modern concepts suggests that death resulted from a dissecting aneurysm of the thoracic aorta. (See page 87.)

18th century John Fothergill (1712–1780), of Edinburgh and London, believed that great and sustained muscular effort resulted in hypertrophy of the heart. (See pages 89, 90.)

18th century John Hunter (1728–1793), of London, believed that the valves of the right side of the heart were not constructed as perfectly as those of the left chambers. This belief was gained by injecting fluids into the pulmonary artery, which resulted in regurgitation of fluid through both valvular barriers. (See pages 91, 92.)

18th century Robert Hamilton (1721–1793), of England, was probably the first to refer to the hereditary factors of angina pectoris. (See page 92.)

18th century Matthew Baillie (1761–1823), of London, showed that death presumably resulting from so-called cardiac polyp was in reality associated with intracardiac thrombi. He mentioned rheumatism of the heart. (See pages 92, 93.)

1788 David Pitcairn (1711–1791), of London, discussed "rheumatism of the heart" but this work was never published. (See page 93.)

1789–1799 Edward Jenner (1749–1823), of Berkeley, Gloucestershire, by careful observation at the bedside and at the postmortem table, related angina pectoris to obliterative arteriosclerosis of the coronary arteries (1799). Ten years earlier Jenner had delivered "Remarks on a disease of the heart following acute rheumatism." This oration was never published and became lost and is historically known as the "lost manuscript." (See pages 94, 95.)

1804 Antonio Scarpa (1747–1832), of Venice, Modena and Pavia, was the first to regard arteriosclerosis as a lesion of the inner coats of the arteries and contended that the

intima and media of arteries were ruptured in aneurysm. (See pages 107, 108.)

1806	Jean-Nicolas Corvisart (1755–1821), of Paris, distinguished between cardiac hypertrophy and dilatation and emphasized the point that an enlarged heart was a diseased heart. He distinguished between organic and functional disturbances of the heart. Corvisart described fibrinous pericarditis and tubercles of the pericardium and recorded an instance of massive pericardial effusion (4 liters). He discussed myocarditis and its frequent association with endocarditis and pericarditis. Corvisart was the first to evolve the concept of pancarditis. (See pages 108, 109.)
1809	Allan Burns (1781–1813), of Glasgow, described the symptoms and the pathologic findings in combined mitral and aortic disease and commented on atrophy of the heart. (See pages 109, 110, 111.)
1810 and 1812	William Charles Wells (1757–1817), of Charleston, South Carolina, and England, described the symptoms of "rheumatism of the heart" and stressed oppression in the thorax, dyspnea, the occasional occurrence of hemoptysis and palpitation and tachycardia. He noted the appearance of albumin in the urine of patients suffering with dropsy. (See page 112.)
1814–1817	Friedrich Ludwig Kreysig (1770–1839), of Berlin, emphasized the fact that a heart showing marked pathologic changes at postmortem examination may have caused remarkably few symptoms while it was equally true that a heart showing few changes may have caused severe symptoms. (See pages 113, 114.)
1st half of the 19th century	Thomas Hodgkin (1798–1866), of Tottenham and London, described arteriosclerosis and made the first systematic attempt to classify the arterial lesions. He recognized three types: those that were cartilaginous, those that were pulpy and those that were purulent. Hodgkin was the first to observe that the vegetations in acute rheumatic endocarditis were located near but not at the edges of the valve leaflets and to call attention to the implantation of acute vegetations by contact of the valve leaflet with the adjacent endocardium. (See page 114.)
1819	René-Théophile-Hyacinthe Laënnec (1781–1826), of Paris, extensively discussed various forms of heart disease including valvular defects, endocarditis, myocarditis, pericarditis and "fatty degeneration of the heart." (See pages 115, 116.)
1824	René-Joseph-Hyacinthe Bertin (1767–1828), of Paris, described valvular vegetations and valvular deformities with special reference to their signs. He gave an excellent account of atrophy of the heart and studied cardiac hypertrophy by means of microscopy. Bertin classified hypertrophy of the heart into three types: concentric, eccentric and simple. (See pages 115, 116.)
1827	Richard Bright (1789–1858), of London, established the nature of nephritis (Bright's disease) and distinguished between renal dropsy and dropsy from other causes. In

	1836 he described cardiac hypertrophy in association with contraction of the kidney in the absence of cardiac valvular disease. (See pages 127, 128.)
1830–1842	Jean Cruveilhier (1791–1873), of Paris, presented colored reproductions of myocardial infarcts but did not ascribe the changes noted to disease of the coronary arteries. He contended, however, that they did not represent infiltration with fat. Cruveilhier held the erroneous belief that phlebitis governed all pathologic processes. (See pages 123, 124.)
1831	James Hope (1801–1841), of Edinburgh and London, described cardiac asthma and wrote on cardiac neurosis. (See pages 121, 122.)
1833	Johann Friedrich Lobstein (1777–1835), of Strasbourg, presented an unusually accurate description of arteriosclerosis. (See page 124.)
1835 and 1841	Jean-Baptiste Bouillaud (1796–1881), of Angoulême and Paris, contributed the "law of coincidence," which stated: "In the great majority of cases of acute generalized febrile articular rheumatism, there exists a variable degree of rheumatism of the fibrous tissue of the heart. This coincidence is the rule and the non-coincidence the exception." He conducted the first accurate study of heart weights and measurements. Bouillaud insisted that myocarditis occurred independently of endocarditis and pericarditis. (See pages 124, 125, 126.)
1st half of the 19th century	William Stokes (1804–1878), of Dublin, described the phenomenon of cardiac displacement which results when a pleural effusion is rapidly absorbed. (See pages 134, 135.)
1850	Sir Richard Quain (1816–1889), of London, regarded the arcus senilis as indicative of infiltration of the myocardium with fat. He reported on 100 cases of cardiac rupture. Quain also called attention to the frequency of cardiac hypertrophy in cases in which the patient had died of apoplexy but did not conceive the relationship of hypertension to cardiac hypertrophy and cerebrovascular accidents. (See pages 146, 147.)
2nd half of the 19th century	Rudolph Ludwig Karl Virchow (1821–1902), of Berlin, believed that an abnormal narrowness of the entire aorta occurred in patients who had chlorosis. He was the first to describe and name endarteritis. Virchow recognized two forms of inflammatory changes in the myocardium, which he classified as parenchymatous and interstitial. He failed to recognize the true significance of the myofibrosis of chronic myocardial ischemia and designated the fibrous changes as "chronic myocarditis." (See pages 151, 152, 153.)
1852	Carl Rokitansky (1804–1878), of Vienna, described atheroma and calcification in the intima of arteries. He was one of the first to make microscopic studies of the fatty heart. (See pages 176, 177.)
1856	Ludwig Traube (1818–1876), of Berlin, published a comprehensive account of the relationship of cardiac and renal disease. He described the symptoms of contracted kidney

and explained the associated hypertrophy of the heart as being the result of increased circulation produced by the diminution of the number of renal capillaries. (See pages 168, 169, 170.)

1862	Maurice-A.-G. Raynaud (1834–1881), of Paris, described the peripheral vascular disturbance which is still known by his name. (See page 158.)
1863	Sir Samuel Wilks (1824–1911), of London, ascribed the myocardial changes in syphilis to two causes: gummata and obliterative endarteritis. (See pages 165, 166.)
1864	Étienne Lanceraux (1829–1910), of Paris, reported the finding of lesions in the cardiac plexus and advanced the belief that neuritis of this plexus was responsible for angina pectoris. He described gummata of the pericardium, discussed chronic myocarditis and stated that it occurred from toxic causes as well as being associated with endocarditis and pericarditis. (See pages 158, 159.)
2nd half of the 19th century	Jacob Mendes DaCosta (1833–1900), of Philadelphia, was of the opinion that severe or recurrent muscular activity was capable of producing cardiac hypertrophy (so-called athlete's heart). (See page 168.)
1866	Adolf Kussmaul (1822–1902), of Heidelberg, Erlangen, Freiburg and Strasbourg, in collaboration with Rudolf Maier, was the first to describe periarteritis nodosa. (See pages 173, 174.)
1872	Sir William Withey Gull (1816–1890), of Colchester and London, conceived the concept of primary arteriolar disease ("hyalin-fibroid") in collaboration with Henry G. Sutton. They discussed the diffuse nature of these vascular changes and the almost universal association of hypertrophy of the left ventricle. Had a practical method existed for the clinical determination of arterial blood pressure, Gull and Sutton might well have recognized the association of hypertension with primary arteriolar disease. Gull, together with Thomas Addison (1793–1860), had described the lesions of xanthelasma. (See page 171.)
1876	Sir William Richard Gowers (1845–1915), of London, was one of the pioneers in the use of the ophthalmoscope and studied the retinal vessels in Bright's disease. In studying the ocular fundi of patients who had Bright's disease he confirmed his impressions of the coexistence of hypertension (determined by means of palpation of the radial pulse) with vascular changes in the retina. (See pages 177, 178.)
1877	Julius Friedrich Cohnheim (1839–1884), of Kiel and Berlin, made his important contribution on paradoxical embolism. He also commented on the so-called idiopathic hypertrophy of the heart. (See pages 179, 180, 181.)
1878	Silas Weir Mitchell (1830–1914), of Philadelphia, described the vasomotor phenomena which became known as "erythromelalgia." (See pages 183, 184.)
1879	Felix von Winiwarter (1852–1931), of Germany, gave the first account of the disease now known as "thrombo-angiitis obliterans." (See page 186.)

1881 Ernest Barié (1848–1931), of France, published an account of traumatic valvular injuries. He separated the lesions into two classes: spontaneous rupture of the valves caused by effort on the part of the patient; and trauma, whereby the injury arose from external violence. (See page 190.)

1882 Carl Weigert (1845–1904), of Münsterberg, Silesia, described tuberculosis of the veins. He also formulated the law that the degree of reparation of injured tissue exceeds the demand. (See page 189.)

1890 Sir Jonathan Hutchinson (1828–1913), of Selby, Yorkshire, and London, described and discussed temporal arteritis and other diseases of the peripheral vessels. (See pages 198, 199.)

1904 Ludwig Aschoff (1866–1942), of Berlin and Freiburg, described the myocardial changes occurring in rheumatic fever. He described the characteristic perivascular cellular changes which still today are known as "Aschoff nodules" or "Aschoff bodies." (See pages 231, 232.)

1908 Leo Buerger (1879–1943), of New York, published his classic article on thrombo-angiitis obliterans (Buerger's disease). (See pages 236, 237.)

1912 Oskar Klotz (1878–1936), of Preston, Ontario, and later of Montreal, Pittsburgh and Toronto, in collaboration with M. F. Manning studied and described the early changes of arteriosclerosis. In 1918, Klotz contributed an important study on the localization of syphilis in the aorta. He showed that the sites of predilection correspond to the regions of abundance of lymphatic vessels. Klotz emphasized the role played by the lymphatics in the slow, yet relentless, transportation of spirochetes. (See pages 246, 247.)

1914 Richard Clarke Cabot (1868–1939), of Boston, was one of the first to call attention to the existing confusion regarding the classification of diseases of the heart and presented a classification based on the pathologic agent or process. (See pages 247, 248.)

1915 Sir Thomas Clifford Allbutt (1836–1925), of Cambridge, discussed the effects of hypertension (hyperpiesia) on the heart. He emphasized the point that the heart is capable of withstanding the increased work imposed by hypertension for long periods before dilatation and hypertrophy supervene. Allbutt extensively discussed the relationship of arteriosclerosis to chronic Bright's disease. (See pages 248, 249, 250.)

1918 Hermann Zondek (1887–), of Berlin, recorded the first comprehensive account of the cardiac changes at times occurring in myxedema. (See pages 252, 253.)

1925 Aldred Scott Warthin (1866–1931), of Ann Arbor, Michigan, expressed the opinion that syphilis of the myocardium is common in spite of the contrary belief held by most pathologists. He brought forth the concept that syphilitic myocarditis could remain silent and latent for years and then suddenly result in death by virtue of an acute exacerbation or "crisis." (See pages 256, 257.)

XIII. THE PERICARDIUM AND ITS DISEASES

4th and 3rd centuries, B.C.	Erasistratus (circa 310–250 B.C.) of Alexandria investigated both the normal and the diseased heart. He searched for the causes of pericarditis and pleuritis. His concept of the cardiovascular system was erroneous and his ideas regarding the causes of disease were based on the factor of plethora (hyperemia). (See pages 13, 14.)
2nd and 3rd centuries, A.D.	Claudius Galen (138–201 A.D.) of Pergamon recognized the occurrence of pericardial effusion and wrote about its embarrassing effects on the activity of the heart. He was apparently the first to consider the tamponade effect of increased quantities of fluid within the pericardial sac. Galen also observed pericardial disease in animals and described a tumor of the pericardium in a monkey. (See pages 16, 17, 18, 19.)
12th century	Avenzoar (1113–1162), of Cordoba, Spain, and Arabia, described scrofibrinous pericarditis and pericardial effusion. (See page 28.)
15th and 16th centuries	Antonio Benivieni (circa 1440–1502), of Padua, described fibrinous pericarditis and commented that the thick stringy deposits of fibrin resembled a structure "loaded with hair." (See page 33.)
16th century	Guillaume de Baillou (1538–1616), of Paris, ascribed palpitation of the heart to effusion in the pericardium. (See page 46.)
Circa 1630	Fabrizio Bartoletti, of Italy, described pericardial adhesions and fatty accumulations in the pericardium. (See pages 56, 57.)
1649	Jean Riolan (Riolanus) (1577–1657), of Paris, was the first to advocate aspiration of the pericardium for effusion. He suggested trephining of the sternum as the approach to the pericardium. No record exists that Riolan practiced this procedure. (See pages 57, 58.)
1669	Richard Lower (1631–1691), of Cornwall, observed the tamponade effect of pericardial effusion and wrote about the restricting action of pericardial adhesions on the heart. (See pages 61, 62.)
1672–1676	Raymond Vieussens (1641–1716), of Montpellier, described pericardial adhesions and commented on their embarrassing effects on cardiac movements and function. He also described the diagnostic features of pericardial effusion. (See pages 75, 76.)
Circa 1700	Giorgio Baglivi (1668–1706), of Rome, described calcification of the pericardium as "of a heart invested in a mortar sheath." (See pages 72, 73.)
1707	Giovanni Maria Lancisi (1654–1720), of Rome, described pericardial adhesions and stressed their clinical importance as a cause of heart disease. (See pages 76, 77.)
1726	Francesco Ippolito Albertini (1662–1738), of Bologna, was aware of the tamponade effect of pericardial effusion and called attention to the fact that the apex pulsation of

the heart became indistinct or disappeared when pericardial effusion was present. (See pages 73, 74.)

1749	Jean-Baptiste de Sénac (1693–1770), of Versailles, discussed the mechanical importance of pericardial adhesions, differentiated between pericardial and pleural effusion and advocated paracentesis for pericardial effusion. (See pages 81, 82.)
1755	Albrecht von Haller (1708–1777), of Bern and Göttingen, described the structure of the pericardium correctly and was the first to describe calcification of the pericardium clearly. (See pages 83, 84, 85.)
1761	John Baptist Morgagni (1682–1771), of Bologna, Padua and Venice, described pericardial effusion, adhesions and calcification. He ascribed dysphagia to pericarditis. (See pages 85, 86.)
1761	Joseph Leopold Auenbrugger (1722–1809), of Vienna, who discovered percussion, utilized this method of examination to demonstrate both pericardial and pleural effusions. (See pages 86, 87.)
1788	David Pitcairn (1711–1791), of London, was the first to relate rheumatism to disease of the heart and especially called attention to the frequency of pericarditis. (See page 93.)
1806	Jean-Nicolas Corvisart (1755–1821), of Paris, gave an excellent account of fibrinous pericarditis and described the massive deposition of fibrin as giving the pericardium the appearance of the reticulum of the second stomach of the calf. He recognized and described tubercles of the pericardium and reported a case of massive pericardial effusion in which the pericardium contained 4 liters of fluid. (See pages 108, 109.)
1809	Allan Burns (1781–1813), of Glasgow, described and discussed pericardial adhesions and stated that at times the pericardium was completely matted to the contiguous structures. (See pages 109, 110, 111.)
1812	John Warren (1753–1815), of Roxbury, Massachusetts, in his discussion of angina pectoris expressed the belief that "ossification" of the coronary arteries was not necessarily the cause of the painful seizures and contended that pericardial adhesions might be responsible. (See page 112.)
1814–1817	Friedrich Ludwig Kreysig (1770–1839), of Berlin, called attention to the systolic retraction of the left half of the epigastrium as a sign of pericardial adhesions. (See pages 113, 114.)
1819	René-Théophile-Hyacinthe Laënnec (1781–1826), of Paris, presented an extensive description of various forms of pericarditis together with their diagnostic signs. (See pages 115, 116.)
Circa 1829	Robert Adams (1791–1875), of Dublin, observed pericardial adhesions in enlarged hearts and expressed the interesting view that the enlargement of the heart resulted from increased vascularity through the adhesions from sources outside of the heart. (See pages 116, 117.)

1829	Dominique-Jean Larrey (1766–1842), of France, was probably the first to perform pericardial incision for effusion. He advocated the epigastric approach to the pericardium. (See pages 119, 120.)
1829–1833	Gabriel Andral (1797–1876), of Paris, in his discussion of acute fibrinous pericarditis stated that the painful symptoms of the disease at times simulated those of angina pectoris. (See pages 120, 121.)
1831	James Hope (1801–1841), of Edinburgh and London, noted pericardial adhesions and commented on their limiting effect on the activity of the heart. (See pages 121, 122.)
1842	Norman Chevers (1818–1886), of London, discussed the compression effects of obliterating pericardial adhesions and was the first to arrive at the modern concept of constrictive pericarditis. He described the manner in which both systole and diastole of the heart were restricted and emphasized particularly the interference with diastole. Chevers held the view that when enlargement of the heart occurred under these circumstances, the enlargement resulted from some other cause such as valvular defects. He was of the opinion that obliterating pericardial adhesions were capable of actually producing atrophy of the heart. (See pages 130, 131.)
1st half of the 19th century	William Stokes (1804–1878), of Dublin, observed that the friction rub in pericarditis could be intensified by gently increased pressure of the stethoscope and at times could be completely obliterated by firm pressure. He also noted the fact that pericarditis at times preceded the involvement of joints in rheumatic fever. Stokes recognized the pain of acute pericarditis and commented that it occasionally simulated the pain of angina pectoris. (See pages 134, 135.)
1861	Armand Trousseau (1801–1867), of Tours and Paris, gave a classic account of the symptoms and signs of pericardial effusion. (See page 157.)
1864	Étienne Lancereaux (1829–1910), of Paris, described gummata of the pericardium in syphilis of the lung. (See pages 158, 159.)
1873	Adolf Kussmaul (1822–1902), of Heidelberg, Erlangen, Freiburg and Strasbourg, extensively investigated mediastinopericarditis (adherent pericarditis) and described the "pulsus paradoxus" as a sign at times present in this disease. (See pages 173, 174.)
2nd half of the 19th century	Julius Friedrich Cohnheim (1839–1884), of Kiel and Berlin, contended that cyanosis and edema occurring in cases of pericardial effusion were due to stasis of blood interfering with the proper oxygenation of the blood. (See pages 179, 180, 181.)
1878	Thomas Morgan Rotch (1849–1914), of Philadelphia, described the absence of resonance on percussion in the fifth right intercostal space, known as "Rotch's sign," as an early sign of pericardial effusion. (See pages 182, 183.)
1881	Luigi Maria Concato (1825–1882), of Italy, described a form of polyserositis with involvement of the pericardium

which became known as "Concato's disease." (See page 190.)

1896 William Ewart (1848–1929), of London, described an area of percussion dullness at the left posterior base of the thorax which he believed was pathognomonic of pericardial effusion. This finding is known as "Ewart's sign." (See page 202.)

1896 Friedel Pick (1867–1926), of Prague, described the clinical syndrome which became known as "Pick's disease." This consisted of pseudocirrhosis of the liver associated with chronic adhesive pericarditis. (See pages 203, 204.)

1897 Sir William Henry Broadbent (1835–1907), of London, described the systolic retraction of the left thoracic intercostal spaces as a sign of adherent pericarditis (Broadbent's sign). (See pages 206, 207.)

1902 Ludolf Brauer (1865–), of Marburg and Heidelberg, advocated the resection of ribs together with the costal cartilages in cases of adherent mediastinopericarditis in which adhesions to the thoracic wall occurred. He referred to the surgical procedure as "Kardiolysis." In Brauer's first two cases the operations were performed respectively by Petersen and by Simon, of Heidelberg. (See pages 226, 227.)

XIV. PHYSIOLOGY OF THE HEART AND CIRCULATION

Circa 1000 B.C.	Author unknown. Ancient China. A medical work, Neiching, stated that the liver stored the blood (soul), the heart stored the pulse (spirit), the spleen stored the nutrition (thought), and the lungs stored the breath (energy) and the kidneys stored the germ principle (will). (See pages 9, 10.)
Circa 500 B.C.	Alcmaeon of Crotona (ancient Greek colony) asserted that the seat of sensation was situated in the brain and not in the heart. In discussing the action of the blood he believed that it was withdrawn from the brain during sleep and flowed to it in greater quantity during periods of wakefulness. (See page 10.)
5th and 4th centuries B.C.	Hippocrates (460–370 B.C.) of Cos (ancient Greece) held the view that the arteries were filled with air while the veins contained blood. (See pages 11, 12.)
4th century B.C.	Plato (427–347 B.C.) (ancient Greece) expressed his ideas regarding the function of the heart and blood vessels. Plato knew that the blood was in constant motion. He referred to body heat as fire and stated that it followed respiration in and out, entered the belly and reached the ingested food by way of the blood. The food was dissolved, separated into fine particles and was then transported into the veins and pumped by the heart through the veins to all parts of the body. (See page 12.)
4th century B.C.	Aristotle (384–322 B.C.) (ancient Greece) believed that the brain constituted a mechanism for cooling the heart and thereby preventing it from becoming overheated. Aristotle also stated that the heart was the first organ to live and the last to die. (See pages 12, 13.)
Circa 300 B.C.	Herophilus of Alexandria believed the arteries to be filled with air. (See page 13.)
4th and 3rd centuries B.C.	Erasistratus (circa 310–250 B.C.) of Alexandria was the first to contend that both the arteries and the veins contained blood. (See pages 13, 14.)
Circa 1st and 2nd centuries A.D.	Rufus of Ephesus (ancient Rome) was apparently the first to note the carotid sinus reflex. He observed that when the arteries of the neck in animals were firmly pressed the animals became drowsy and "lost voice." Rufus believed that these phenomena did not occur from pressure on the arteries but rather from pressure on the contiguous nerves. (See page 15.)
2nd and 3rd centuries A.D.	Claudius Galen (138–201 A.D.) of Pergamon described his fantastic and erroneous concept of the heart and blood vessels which was quite universally accepted for nearly fourteen centuries. He believed that the blood was formed in the liver from ingested food and conveyed by the veins to the right side of the heart and by a process of ebb and flow back to the liver. It was then transported to all parts of the body by other veins. A small quantity of blood remained in the right side of the heart and ultimately

reached the left side of the heart by way of "invisible pores" in the interventricular septum. Galen's anatomic experience was largely derived from dissections on animals, although it is possible that he carried out some human dissections. His anatomic concepts were a conglomeration of ideas derived from observation of animal and human structures and his sustaining physiologic ideas were speculative and based on the necessity of validating his erroneous and incomplete anatomic data. (See pages 16, 17, 18, 19.)

12th century — Avenzoar (1113–1162), of Cordoba, Spain, and Arabia, commented on the relative importance of the right and the left ventricles, and concluded that the latter was the most important. (See page 28.)

13th century — Ibn an-Nafis, ancient Arabian physician, wrote a commentary on Avicenna's "Anatomy," wherein, by utilizing speculation and logic, he correctly deduced the general scheme of the pulmonary circulation. Ibn an-Nafis denied the existence of "invisible pores" in the interventricular septum as taught by Galen. (See pages 28, 29, 30.)

1450 — Nicholas Krebs (Cardinal Cusanus) (1401–1464), of Cues, Germany, in his "Dialogue of statics" counted the respirations in health and disease. He advocated carrying out estimations of the weight of the blood and urine which probably constituted the first concept of biologic measurement. Krebs's suggestions were not carried out for many generations. (See page 32.)

15th and 16th centuries — Leonardo da Vinci (1452–1519), the early Italian genius, conceived the heart as a pump. (See pages 33, 34, 35, 36.)

1522 — Jacopo Berengario da Carpi (1470–1550), of Bologna and Farrara, conducted one of the earliest experiments concerned with the injection of arteries. He filled them with tepid water in order to follow their course. (See page 36.)

Circa 1543 — Andreas Vesalius (1514–1564), of Padua, demonstrated that the life of an animal could be sustained by artificial respiration after the thorax had been opened. He also showed that the nonbeating heart could at times be resuscitated by means of bellows. (See pages 38, 39.)

1553 — Michael Servetus (1509–1553), of Villanueva de Sigena, Spain, the martyr, discussed the existence of the pulmonary circulation. (See page 40.)

1559 — Matteo Realdo Colombo (Columbus) (1516?–1559), of Cremona, described the pulmonary circulation but did not correctly conceive all its details. He maintained Galen's belief that the veins conveyed the nutritive blood and that the liver was the central organ of the cardiovascular system. By means of experiments on animals, Colombo proved that the pulmonary veins contained blood but held the belief that the blood became cooled during the process of respiration. (See page 42.)

1571–1593 — Andrea Cesalpino (1519 or 1524–1603), of Arezzo and Pisa, by means of dissection, observation and logical de-

ductions conceived the general scheme of the circulation of the blood. (See pages 43, 44.)

1628 — William Harvey (1578–1657), of Folkestone and London, in his masterly work, "Exercitatio anatomica de motu cordis et sanguinis in animalibus," described both the anatomy and the general physiologic principles of the systemic and pulmonary circulations. He predicted the existence of the capillary circulation. Harvey is generally regarded as the discoverer of the circulation, although records show that Ibn an-Nafis, Servetus and Cesalpino had made important contributions which have largely been ignored. (See pages 44, 45.)

1661 — Marcello Malpighi (1628–1694), of Bologna and Pisa, by means of microscopy demonstrated the capillaries and the structure of the lungs. (See page 59.)

1669 — Richard Lower (1631–1691), of Cornwall, contributed to knowledge of the physiology of respiration. After injecting dark venous blood into insufflated lungs he noted its subsequent red color and concluded that the change was due to the fact that the blood had absorbed some of the air passing through the lungs. He also demonstrated anastomoses between coronary arteries by experimentally injecting one artery from another. Lower studied the systolic contraction of the heart and considered the heart to be a muscle. (See pages 61, 62.)

1674 — John Mayow (1643–1679), of Cornwall, while working with a gas which he had obtained from niter and which he designated as "nitro-aerial spirit," noted that the dark venous blood became red when it was placed in contact with this gas. Mayow did not realize that he had nearly discovered oxygen. He also described the function of the intercostal muscles as accessory muscles of respiration. He was the first to indicate the muscles of the body as the seat of animal heat. (See pages 62, 63.)

1677 — Jan Swammerdam (1637–1680), of Holland, studied the movements of the heart, lungs and muscles by primitive plethysmographic methods. He concluded that a muscle does not increase its bulk during contraction. He injected materials of low melting points (wax) into vessels to enable him to study the finer tributaries and anastomoses of vessels. (See page 63.)

1680–1681[*] — Giovanni Alfonso Borelli (1608–1679), of Pisa, was interested in the physiology of muscles, including the heart muscle. He believed that the contracting muscle increased its bulk owing to a fermentative process occurring in the muscle substance. Borelli further held the view that the nerve supplying the muscle discharged a fluid (succus nerveus) into the substance of the muscle. (See page 64.)

1698 — Pierre Chirac (1650–1732), of France, was apparently the first to investigate the effect of ligation of a coronary artery in the dog. He concluded that the procedure produced cardiac standstill. (See page 66.)

[*] Posthumous publication.

1700	Giorgio Baglivi (1668–1706), of Rome, conducted experiments on the physiology of muscles and was the first to recognize and distinguish the differences between smooth and striated muscle. He cut the vagi in the neck of a dog and observed that the animal was unable to bark and had periodic dyspnea and vomiting. (See pages 72, 73.)
1703–1712	Antony van Leeuwenhoek (1632–1723), of Delft, studied the vascular system of fishes and erroneously stated that pulsations occurred in the veins and not in the arteries. He confirmed Malpighi's findings regarding the existence of the capillary circulation. (See pages 64, 65.)
1705	Raymond Vieussens (1641–1716), of Montpellier, advanced the idea that the coronary vessels have direct communication with the chambers of the heart. (See pages 75, 76.)
1708	Adam Christianus Thebesius (1686–1732) injected materials into the coronary vessels and observed their passage into the chambers of the heart through small orifices in the endocardium. He erroneously believed that the aortic semilunar valves closed the openings of the coronary arteries during ventricular systole. (See page 78.)
1726	Francesco Ippolito Albertini (1662–1738), of Bologna, conceived the general factors operative in heart failure and differentiated pulmonary congestion, pulmonary edema and hydrothorax. (See pages 73, 74.)
*1728**	Giovanni Maria Lancisi (1654–1720), of Rome, injected mercury into the coronary arteries of experimental animals and observed that it appeared in the chambers of the heart. He speculated that the mercury escaped through venous channels. (See pages 76, 77.)
1733	Stephen Hales (1677–1761), of Beckesbourne, Kent, and Teddington, Middlesex, conducted ingenious but crude experiments on animals dealing with the hydrostatics of the circulation. He estimated arterial and venous blood pressure and blood velocity. (See pages 80, 81.)
18th century	Albrecht von Haller (1708–1777), of Bern and Göttingen, noted the changes that occurred in the heart during systole, demonstrated the property of irritability of muscles and proved the automatism of the heart. He attributed the alternate distention and collapse of the jugular veins to the effect of gravity and the respiratory aspiration of the thorax. (See pages 83, 84, 85.)
1761	John Baptist Morgagni (1682–1771), of Bologna, Padua and Venice, studied the pulsations of the jugular veins and ascribed one impulse to contraction of the auricle and the other to contraction of the ventricle. (See pages 85, 86.)
1777	Lazaro Spallanzani (1729–1799), of Scandiano, was the first to show that the impetus given to the blood by the contraction of the heart was maintained throughout the entire arterial system as far as the smallest capillary. He studied the capillary circulation, observed the circulation through the lungs and noted the velocity of the blood and

* Posthumous publication.

the arterial dilatation produced by systole of the ventricle. Spallanzani further observed that a heart chamber emptied itself during systole. His investigations also included the respiratory gaseous exchange in warm-blooded and cold-blooded animals. (See page 89.)

18th century

Antoine-Laurent Lavoisier (1743–1794), of France, demonstrated that respiration caused chemical alterations in the inspired air, that some of the air which entered the lungs did not come out as such and that some of the oxygen, or "vital air" as he called it, was absorbed by the blood. (See page 90.)

1798

John Abernethy (1764–1831), of London, confirmed the experiments of Vieussens and Thebesius. By making a "common coarse waxen injection" into the coronary arteries he observed that the wax flowed readily into the chambers of the heart. (See page 94.)

1816

Caleb Hillier Parry (1755–1822), of Bath, concluded correctly that the pulse wave is caused by the impulse given to the blood by the systole of the left ventricle. (See pages 95, 96.)

1819

René-Théophile-Hyacinthe Laënnec (1781–1826), of Paris, correctly recognized that the first sound of the heart coincided with systole of the ventricle but erroneously believed that the second heart sound occurred with systole of the auricle. (See pages 115, 116.)

Circa 1830

Robert Adams (1791–1875), of Dublin, evidently possessed a remarkably advanced concept regarding certain phases of the mechanics of heart failure, for he contended that the development of regurgitation at the tricuspid valve relieved stasis in the pulmonary circulation. (See pages 116, 117.)

1831

James Hope (1801–1841), of Edinburgh and London, investigated the mechanism of production of the heart sounds. He examined the hearts of stunned donkeys the respiration of which had been artificially sustained after the pericardium had been opened and proved that the second heart sound is dependent on the abrupt closure of the aortic and pulmonary valves. (See pages 121, 122.)

1835

Charles J. B. Williams (1805–1889), of England, expressed the opinion that the first sound of the heart was produced by muscular contraction because in an experiment on the heart of an ass from which the blood had been removed, the first sound was still audible during cardiac systole. He reasoned erroneously that under these circumstances the valve leaflets did not move. (See page 126.)

1st half of the 19th century

Joseph Skoda (1805–1881), of Pilsen and Vienna, contended that the apex beat of the heart was produced by the recoil of the heart which resulted from the column of blood projected into the aorta. (See page 128.)

1842

John E. Erichsen (1818–1896), of London, ligated the coronary arteries of dogs and rabbits and found that death of the animals occurred within ten minutes. He concluded from these experiments that any disease, such as "ossification" of the coronary arteries, that interferes with the

flow of blood through them may result in sudden death. (See page 130.)

1845 Ernst Heinrich Weber (1795–1878), of Wittenberg and Leipzig, and his brother, Eduard Friedrich Weber (1806–1871), made the important discovery proving the cardio-inhibitory action of the vagus. In earlier contributions the brothers had measured the velocity of the pulse wave for the first time and somewhat later measured and compared the velocity of the blood and lymph corpuscles in the capillaries. (See page 133.)

Circa 1845 Carl Ludwig (1816–1895), of Marburg, Zurich and Leipzig, introduced the graphic method of physiologic investigation by the use of such apparatus as the kymograph, blood pump and Stromuhr. He was a pioneer in perfusion experiments on excised organs. Ludwig advanced the hypothesis that lymph is formed by the diffusion of fluids from the blood through the walls of the vessels into the surrounding tissues, the hydrostatic force producing this phenomenon being the capillary blood pressure. He discussed arterial blood pressure. (See page 136.)

1852 Hermann Stannius (1808–1883), of Hamburg, applied a ligature at the junction of the auricle and the sinus venosus of the frog's heart which resulted in standstill of the heart. The application of a second ligature to the auriculo-ventricular groove caused the ventricles to beat again. In this experiment, Stannius demonstrated the important fact that the ventricles are endowed with the property of initiating their own rhythm in heart block (idioventricular rhythm). (See page 149.)

1854 Claude Bernard (1813–1878), of Paris, demonstrated the vasomotor nerves and their mechanism. Later he demonstrated that the sympathetics are the nerves of vasoconstriction and the chorda tympani is the nerve of vasodilatation. (See pages 147, 148.)

2nd half of the 19th century Sir Michael Foster (1836–1907), of Cambridge, demonstrated that any part of the heart separated from the rest will beat rhythmically. He also showed that the heart destitute of its ganglia continues to beat in a perfectly normal manner. Foster concluded that rhythmicity is a specific and inherent quality of heart muscle in general and not of any one localized portion or of its innervation. (See pages 153, 154.)

1862 Peter Ludwig Panum (1820–1885), of Kiel and Copenhagen, confirmed Erichsen's experiments but instead of ligating the coronary arteries he utilized the method of experimental emboli. While death of the animals occurred, the cessation of cardiac action was gradual rather than abrupt. (See page 157.)

1870 and 1882 Adolf Fick (1829–1901), of Kassel, conducted extensive experiments (1870) on blood flow and later (1882) investigated methods of estimating the work and the output of the heart. He measured the pressure within the chambers of the heart. (See pages 166, 167.)

1871 Ludwig Traube (1818–1876), of Berlin, presented a concise description of pulsus bigeminus, its mechanism and

significance. He concluded that the phenomenon occurs with failure of the left ventricle and cited an instance in which digitalis apparently contributed to its appearance. (See pages 168, 169, 170.)

1875	Heinrich Irenaeus Quincke (1842–1922), of Berlin and Kiel, demonstrated that pressure on the carotid artery in the neck produced slowing of the heart and explained this phenomenon on the basis of stimulation of the vagus nerve. Note early mention of this phenomenon by Rufus of Ephesus. (See pages 163, 164.)
2nd half of the 19th century	Henry Pickering Bowditch (1840–1911), of Boston, conducted important experiments with reference to the physiology of heart muscle. By direct electrical stimulation of the myocardium with uniform intensity and frequency, he found that the first few contractions decreased slightly but after this initial fall, the contractions increased with remarkable regularity. This gradual increase in the extent of muscular shortening with a constant stimulus led Bowditch to name this behavior "treppe" or "staircase phenomenon." After this period had been passed, the contractions were found to diminish steadily until muscular fatigue ensued and no further response to stimulation occurred. Bowditch also demonstrated the important fact that the heart liberates all of its available energy at each contraction. This phenomenon is known as the "all or none" law of Bowditch. (See page 167.)
1876–1878	Étienne-Jules Marey (1830–1904), of Paris, was a pioneer in the study of blood pressure and the creator of a sphygmograph. He devised the first reasonably useful apparatus for estimating arterial blood pressure in man. Marey stated that the maximal pressure (systolic) may be determined as the point where the pulsation disappears and the minimal pressure (diastolic) as the point where the oscillations are of greatest magnitude. Marey demonstrated the fundamental fact that the maximal excursion of the pulse wave was obtained when the pressure about the artery was equal to the pressure within the artery. He also devised a sphygmograph with two tambours, so that two simultaneous pulse records could be obtained. (See pages 178, 179.)
2nd half of the 19th century	Julius Friedrich Cohnheim (1839–1884), of Kiel and Berlin, was one of the first exponents of the belief that the normal heart is possessed of great amounts of reserve power. He also showed that when large quantities of sodium chloride were introduced into the blood stream of dogs, increased transudation of fluid into the tissues occurred. (See pages 179, 180, 181.)
1878	William Henry Welch (1850–1934), of New York and Baltimore, conducted experiments dealing with the mode of production of pulmonary edema. He concluded that edema of the lungs occurred when the outflow of the blood from the left ventricle was impeded, as in failure of the ventricle. The blood, continuing to reach the lungs from the right ventricle, which was still functioning adequately, caused an increased pressure within the pul-

monary circuit. This resulted in stasis and the seepage of fluid and cells into the alveoli of the lungs. The rapid occurrence of these events together with the remarkable permeability of the pulmonary capillaries favored the ready development of pulmonary edema. (See pages 185, 186.)

1881 Walter Holbrook Gaskell (1847–1914), of Cambridge, proved that the rhythmic contractile power of the heart was autonomous and was inherent in the heart muscle itself. In 1874 he described the vasomotor nerves of striated muscle. Later, Gaskell demonstrated the vasoconstrictor and vasodilator nerves. He showed that the innervation of the heart is the same in both warm-blooded and cold-blooded animals and that vagal stimulation depresses as well as slows the heart. (See page 191.)

1894 William Townsend Porter (1862–), of Cambridge, Massachusetts, conducted experiments on ligation of the coronary arteries. He noted that the procedure frequently resulted in fibrillary contractions of the heart and sudden death. However, death did not always occur and this led him to conclude that Cohnheim's (1881) consistently fatal results were due to operative trauma and that the coronary arteries were not end arteries. (See page 203.)

1899 Walter Baumgartner, working in Porter's laboratory, repeated Porter's experiments and produced infarcts of the myocardium. (See page 203.)

1910 Sir Thomas Lewis (1881–1945), of London, proved by means of electrocardiography that the cardiac impulse has its origin in the sino-auricular node (node of Keith and Flack). (See pages 241, 242.)

1914 Ernest Henry Starling (1866–1927), of London, established his famous "law of the heart." In collaboration with S. W. Patterson and H. Piper, of Berlin, Starling demonstrated the mechanism involved in the adjustment of the heart to the demands of increased work. (See page 248.)

1919 August Krogh (1874–), of Copenhagen, made extensive investigations on the physiology of the capillaries. His investigations were so meritorious that he was awarded the Nobel Prize in 1920. (See pages 253, 254.)

XV. THE PULSE

3000–2500 B.C.	Imhotep (?) (Edwin Smith Surgical Papyrus, discovered in 1862) associated the pulse with the beat of the heart and is believed to have counted the pulse by means of a water clock. (See pages 6, 7.)
6th and 5th centuries B.C.	Pien Ch'iao (ancient China) is believed to be the originator of Chinese pulse lore. (See page 9.)
5th and 4th centuries B.C.	Hippocrates (460–370 B.C.) of Cos counted the pulse. (See pages 11, 12.)
5th and 4th centuries B.C.	Aegimius, a contemporary of Hippocrates, discussed the movement of the arteries and undoubtedly used this expression in alluding to the pulse. (See page 12.)
Circa 340 B.C.	Praxagoras of Cos observed the synchronism of the pulse and the beat of the heart. (See page 13.)
Circa 300 B.C.	Herophilus of Alexandria is generally credited as being the first to count the pulse, although history records several predecessors. He commented on the systolic and diastolic phases of the pulse and described four cardinal properties of the pulse: frequency, rhythm, size and strength. Herophilus apparently was the first to describe the peculiar pulse, "pulsus caprizans" (like the leap of a goat), which consisted of an initial stroke believed to result from only partial dilatation of the artery, immediately followed by a more forceful stroke. Perhaps Herophilus had noted the extrasystole or the dicrotic pulse. (See page 13.)
Circa 1st and 2nd centuries A.D.	Rufus of Ephesus, ancient Roman, asserted that the pulse was synchronous with the beat of the heart. He noted the size, frequency, strength and resistance of the pulse. Rufus also stated that the movements of the fontanelles in infants were produced by arterial pulsations. (See page 15.)
1st and 2nd centuries	Archigenes (circa 54–117), a Greek practicing medicine in Rome, wrote about the pulse. His concepts of health and disease were based on the doctrines of "pneuma." "Pneuma" was considered the basis of health and with this factor in balance, proper tonus was maintained and could be detected by the pulse. Archigenes believed that the pulse beat consisted of four phases: contraction, dilatation and two periods of rest. (See page 15.)
1st century	Charaka (early in the first century), ancient Buddhist, was aware of the synchronism of the pulse with the beat of the heart. He also observed that the pulse disappeared when death occurred. (See page 16.)
2nd and 3rd centuries	Claudius Galen (138–201) of Pergamon wrote extensively but erroneously on the pulse. He believed that alterations in the pulse were the result of mild dyscrasias and that sudden death resulted from severe or organic dyscrasias. (See pages 16, 17, 18, 19.)
280	Author unknown. Mei Ching or the Book of the Pulse is probably the work referred to by Michael Boym, a Jesuit missionary, in 1666. (See page 10.)

7th century	Paul of Aegina (625–690) (ancient Greece) wrote an extensivé work on the pulse and widely quoted the observations and beliefs of Galen. (See page 19.)
Time unknown	Kanáda, an Indian philosopher, wrote a treatise on the pulse. (See page 19.)
9th and 10th centuries	Rhazes (865–925), a Persian physician, discussed the importance, when rendering a prognosis, of studying alterations of the pulse, of the action of the heart, of respiration and of body excretions. (See page 20.)
10th and 11th centuries	Avicenna (980–1037), a Persian physician, wrote extensively on the pulse. He misinterpreted, yet supported, many of Galen's erroneous ideas. (See page 20.)
1450	Nicholas Krebs (Cardinal Cusanus) (1401–1464), of Cues, Germany, published his "Dialogue of statics," which contained observations on the pulse, and commented that he counted the pulse by means of a water clock. (See page 32.)
15th century	Bartolommeo Montagnana (?–1460), of Padua, described an abnormal rhythm of the pulse which he referred to as "motus tremulans et bipulsans cordis." This may have been auricular fibrillation. (See page 28.)
15th and 16th centuries	Leonardo da Vinci (1452–1519), the early Italian genius, contended that the pulse was synchronous with the beat of the heart. (See pages 33, 34, 35, 36.)
1523	Thomas Linacre (1460–1524), of England, wrote a treatise on the pulse which was largely a translation of Galen's works. (See page 36.)
16th and 17th centuries	Prosper Alpinus (1553–1617), of Padua, described the principal causes of the pulse which according to his concepts comprised the necessity of pulsation, the vital factor or function, and the subservience of the pulse to the faculty. (See page 45.)
1600	Johann Kepler (1571–1630), the great German astronomer, utilized the pulse count in his astronomic observations. (See page 54.)
16th and 17th centuries	Galileo Galilei (1564–1642), the famous Italian astronomer, used his own pulse count to test the regularity of the swing of a pendulum and later reversed the procedure to count the pulse by means of a pendulum. (See page 54.)
1625	Santorio Santorio (Sanctorius) (1561–1636), of Capodistria, devised a pulse clock which consisted of a weight suspended on a thread. The weight was allowed to oscillate like a pendulum. The oscillations increased in frequency as the thread was shortened and this procedure was repeated until the frequency of oscillation of the weight was equal to the frequency of the pulse. The free length of the thread was then measured on an appended scale and the pulse rate was computed therefrom. (See page 54.)
1630	Robert Fludd (1574–1637), of England, wrote a voluminous treatise on the pulse which was largely composed of ancient data with comments of his own. (See page 57.)

1683 Lorenzo Bellini (1643–1704), of Pisa, wrote a treatise emphasizing the importance of studying the pulse and the urine in both health and disease. (See page 64.)

1695 Raymond Vieussens (1641–1716), of Montpellier, commented on the water-hammer pulse in aortic insufficiency. (See pages 75, 76.)

1707 Sir John Floyer (1649–1734), of Staffordshire and Lichfield, invented a pulse watch designed to run precisely one minute. (See page 77.)

1816 Caleb Hillier Parry (1755–1822) wrote an extensive treatise on the pulse. While some of his conclusions were erroneous, he, nevertheless, concluded correctly that the pulse wave is caused by the impulse given to the blood by the systole of the left ventricle. (See pages 94, 95.)

1868 Heinrich Irenaeus Quincke (1842–1922), of Berlin and Kiel, was the first to make detailed studies of the capillary pulse and to note its significance in the diagnosis of aortic insufficiency. (Sec pages 163, 164.)

1871 Ludwig Traube (1818–1876), of Berlin, presented a concise description of pulsus bigeminus, its mechanism and significance. He concluded that the phenomenon occurs with failure of the left ventricle and cited an instance in which digitalis apparently contributed to its appearance. (See pages 168, 169, 170.)

1873 Adolf Kussmaul (1822–1902), of Heidelberg, Erlangen, Freiburg and Strasbourg, extensively investigated mediastinopericarditis (adherent pericarditis) and described the "pulsus paradoxus" as a sign at times present in this disease. (See pages 173, 174.)

XVI. SURGERY OF THE HEART AND BLOOD VESSELS

1564 Ambroïse Paré (1510–1590), of Paris, advised against incising superficial peripheral tumors (which frequently proved to be aneurysms) and deplored the application of corrosive agents. He suggested careful exploration of such tumors and, when they were proved to be saccular aneurysms, described a method whereby the sac could be ligated. (See page 41.)

1594 Jacques Guillemeau (1550–1613), of France, was the first to use the single ligature in the treatment of peripheral aneurysm. (See page 46.)

1649 Jean Riolan (Riolanus) (1577–1657), of Paris, was the first to advocate aspiration of the pericardium for effusion. He suggested trephining of the sternum as the approach to the pericardium. No record exists that Riolan practiced this procedure. (See pages 57, 58.)

1710 Dominique Anel (1628–1725), of Toulouse, recorded the second instance of treating aneurysm by the method of single ligation. (See pages 78, 79.)

1785 John Hunter (1728–1793), of London, devised and performed his famous operation for aneurysm, which consisted in ligation of the artery at a point beyond the dilatation. However, Jacques Guillemeau had performed this procedure in 1594 and Dominique Anel had also applied the single ligature in 1710. (See pages 91, 92.)

1796 John Abernethy (1764–1831), of London, was the first to ligate the external iliac artery for aneurysm. In 1809 he reported four cases in which the procedure had been employed, twice with success. In 1798 Abernethy ligated the common carotid artery for hemorrhage. (See page 94.)

*1801** Pierre-Joseph Desault (1744–1795), of Paris, was another pioneer in the surgical treatment of aneurysm. He advocated the distal ligation of aneurysms. (See page 107.)

1808 Sir Astley Paston Cooper (1768–1841), of Norfolk and London, successfully ligated the common carotid and the external iliac arteries for aneurysm. Nine years later he performed the then unbelievable feat of ligation of the abdominal aorta. (See page 109.)

1829 Dominique-Jean Larrey (1766–1842), of France, was probably the first to perform pericardial incision for effusion. He advocated the epigastric approach to the pericardium. (See pages 119, 120.)

1830 Alfred-Armand-Louis-Marie Velpeau (1795–1867), of Paris, was the first to attempt to obliterate the sac of aneurysms by the production of mural thrombosis. He suggested the insertion of needles into the aneurysmal sac with the intention of producing local irritation with consequent formation of a thrombus. (See page 120.)

* Posthumous publication.

1832 — Benjamin Phillips (1805–1861), of London, employed Velpeau's method. (See page 120.)

1835 — Charles J. B. Williams (1805–1889), of England, reported the successful surgical closure of a stab wound of the heart. (See pages 126, 127.)

2nd half of the 19th century — Paul Broca (1824–1880), of Paris, was the first to recognize the potential dangers of arteriovenous fistula and to approach the condition from the surgical standpoint. (See pages 149, 150.)

1864 — Charles Hewitt Moore (1821–1870) and Charles Murchison (1830–1879), of London, devised a new method of treating aneurysms. With the intention of producing mural thrombosis and ultimate organization of the thrombus within the sac of the aneurysm, they passed fine wire into the sac and allowed it to remain there. This method did not prove to be effective. (See page 159.)

1873 — George William Callender (1830–1878), of London, published what appears to be the first authenticated account of the successful removal of a foreign body (needle) from the human heart. (See page 174.)

1874 — Thomas Bevill Peacock (1812–1882), of London, published a report on a dissecting aneurysm of the aorta which was discovered at postmortem examination. The patient was a sixty-one year old actor whose death occurred suddenly following a severe but brief episode of precordial pain. (See page 159.)

1879 — Pietro Burresi (1822–1883) and G. Corradi (1830–1907), of Italy, applied the wiring method of Moore and Murchison (1864) in the treatment of aneurysm and passed an electric current through the wire to produce mural thrombosis. This method of electrocoagulation became known as the Moore-Corradi method. (See pages 188, 189.)

1896 — Guido Farina, of Italy, sutured a penetrating wound of the heart. The suture was successful although the patient died from complicating pneumonia on the eighth day. Farina proved that suture of wounds of the heart is possible. (See page 205.)

1896 — Louis Rehn (1849–1930), of Frankfurt am Main, performed a successful suture of a stab wound of the heart. The case was not reported until 1907, at which time the patient was still alive. (See pages 205, 206.)

1898 — Edmond Delorme (1847–1929), of Paris, who had been the first to perform decortication of the lungs in cases of chronic empyema, recommended removal of the pericardium in cases of adhesive pericarditis. (See page 207.)

1902 — Rudolph Matas (1860–   ), of New Orleans, is an American pioneer in surgery of the vascular system. In 1888 he published his first account of a new method for the surgical cure of aneurysm. However, the first comprehensive account of the new method, "endo-aneurysmorrhaphy" or "intrasaccular suture," appeared in 1902. Dr. Matas is the author of 108 important articles

1902 dealing with surgery of the vascular system. (See pages 225, 226.)

Ludolf Brauer (1865–   ), of Marburg and Heidelberg, advocated the resection of ribs together with the costal cartilages in cases of adherent mediastinopericarditis in which adhesions to the thoracic wall occurred. He referred to the surgical procedure as "Kardiolysis." In Brauer's first two cases the operations were performed respectively by Petersen and by Simon, of Heidelberg. (See pages 226, 227.)

1907 John C. Munro (1858–1910), of Boston, predicted the feasibility of surgical ligation of the patent ductus arteriosus. He described a method which he had employed during a postmortem examination in a case of this congenital abnormality. (See page 225.)

1916 Thomas Jonnesco (1860–1926), of France, was the first to proclaim the curative effects of cervical sympathectomy in cases of angina pectoris. His first report was published four years after the first operation had been performed. In analyzing Jonnesco's case report it is very doubtful whether the patient was suffering from angina pectoris with coronary sclerosis; in all probability he had syphilitic aortitis with painful seizures. (See page 255.)

XVII. SYMPTOMS OF DISEASES OF THE HEART AND CIRCULATION

5th and 4th centuries B.C.	Hippocrates (460–370 B.C.) of Cos described the facies of impending death (Hippocratic facies). He also described that peculiar form of respiration which many centuries later was to become known as Cheyne-Stokes respiration. Hippocrates stated that sudden death was more likely to occur in obese than in thin persons. (See pages 11, 12.)
5th and 4th centuries B.C.	Aegimius, a contemporary of Hippocrates, is said to have written a treatise on palpitation of the heart. (See page 12.)
1st century A.D.	Lucius Annaeus Seneca (4 B.C.–65 A.D.) presented a vivid description of his own symptoms of the disorder which many centuries later was to be named "angina pectoris." (See page 15.)
7th century	Paul of Aegina (625–690) (ancient Greece) designated syncope as a symptom of heart disease. (See page 19.)
15th century	Bartolommeo Montagnana (?–1460), of Padua, designated cough as a symptom of heart disease. He undoubtedly had observed the passive pulmonary congestion of heart failure. (See page 28.)
16th century	Guillaume de Baillou (1538–1616), of Paris, ascribed palpitation of the heart to effusion in the pericardium. (See page 46.)
1707	Giovanni Maria Lancisi (1654–1720), of Rome, was aware of the symptoms of the disorder later to be known as "angina pectoris" and its relation to sudden death. He related sudden death to structural changes in the heart and related syncope to nervous affections of that organ. (See pages 76, 77.)
1707	Friedrich Hoffmann (1660–1742), of Halle, described convulsive asthma associated with dropsy and speculatively related these phenomena to the heart. In 1753 a posthumous book by Hoffmann described the syndrome of angina pectoris without ascribing a name or a cause to the symptoms. (See pages 77, 78.)
1710	Pierre Dionis (?–1718), of Paris, reported two cases of painful disorder of the thorax which he ascribed to disease of the heart and which may well have been examples of the anginal syndrome of coronary disease. (See page 78.)
1726	Francesco Ippolito Albertini (1662–1738), of Bologna, related pains in the arms and shoulders to heart disease and emphasized the importance of dyspnea as a symptom. (See pages 73, 74.)
1749	Jean-Baptiste de Sénac (1693–1770), of Versailles, discussed asthma in relation to heart disease and called attention to orthopnea and edema of the legs, as manifestations of heart failure. (See pages 81, 82.)

1761	John Baptist Morgagni (1682–1771), of Bologna, Padua and Venice, ascribed dysphagia to aneurysm and pericarditis. He believed that cyanosis resulted from venous stasis rather than from the intermingling of arterial and venous blood. (See pages 85, 86.)
*1802**	William Heberden (1710–1801), of London, described and named the clinical syndrome which has since been known as "angina pectoris" or, as he expressed it, "pectoris dolor." He believed the painful syndrome to be due to spasm of the heart. The work was not published until a year after Heberden's death. (See pages 87, 88.)
1810 and 1812	William Charles Wells (1757–1817), of Charleston, South Carolina, and England, described the symptoms of "rheumatism of the heart" and stressed oppression in the thorax, dyspnea, the occasional occurrence of hemoptysis, palpitation and tachycardia. (See page 112.)
19th century	Jean-Nicolas Corvisart (1755–1821), of Paris, separated heart failure into three stages and discussed the relationship of valvular lesions to the development of heart failure. (See pages 108, 109.)
1818	John Cheyne (1777–1836), of Edinburgh and Dublin, was the first to describe that periodic type of breathing later to be known as "Cheyne-Stokes respiration." (See pages 114, 115.)
*1825**	Caleb Hillier Parry (1755–1822), of Bath, is well known for his observations on exophthalmic goiter and his description of the circulatory phenomena accompanying it. (See pages 95, 96.)
1836	John Calthrop Williams (19th century), of Edinburgh, wrote a treatise on nervous and sympathetic palpitation of the heart. (See pages 127, 128.)
1845–1846	Peter Mere Latham (1789–1875), of London, was the first to emphasize the sense of impending death which at times accompanies the anginal syndrome. Earlier, Latham had reported a group of cases in which sudden death did not occur in spite of the occurrence of severe seizures of angina pectoris and designated this condition as "pseudo-angina." (See page 134.)
1854	William Stokes (1804–1878), of Dublin, gave a lucid account of the periodic type of breathing discussed by John Cheyne in 1818 and this phenomenon is still known as "Cheyne-Stokes respiration." (See pages 134, 135.)
1866	Thomas Bevill Peacock (1812–1882), of London, favored the belief that cyanosis in congenital heart disease resulted from venous stasis rather than from the admixture of venous and arterial blood. (See page 159.)
1867	Sir Thomas Lauder Brunton (1844–1916), of Edinburgh and London, in considering cardiac pain in general expressed the opinion that it was the result of weakness of the heart and occurred in proportion to the resistance which the organ was required to overcome. He ascribed angina pectoris specifically to vascular spasm of the vessels of the heart. (See pages 159, 160.)

* Posthumous publication.

2nd half of the 19th century	Hermann Nothnagel (1841–1905), of Freiburg, Jena and Vienna, ascribed pain to valvular lesions and reported on the relative frequency of this symptom according to the valve or valves involved. (See page 161.)
1871	Jacob Mendes DaCosta (1833–1900), of Philadelphia, gave the first accurate account of neurocirculatory asthenia based on data which he had acquired from observations on soldiers during the Civil War. (See page 168.)
2nd half of the 19th century	Ludwig Traube (1818–1876), of Berlin, discussed Cheyne-Stokes respiration and attributed this phenomenon to a diminished supply of arterial blood to the medulla which resulted in the deprivation of the respiratory center of an adequate amount of oxygen. (See pages 168, 169, 170.)
1901 and 1905	Harry Orville Hall, of Washington, D. C., recorded important observations dealing with the cerebral manifestations of digitalis intoxication. (See pages 224, 225.)

XVIII. THERAPY OF THE HEART AND CIRCULATION

Circa 1st century A.D. Pedacius Dioscorides (ancient Greece) in his six volume work on poisons and antidotes (De universa medicina) listed squill. No record exists to the effect that this drug was used for disorders of the heart. (See page 10.)

1st century Aurelius (Aulus) Cornelius Celsus, early Roman encyclopedist, discussed the treatment of "kardiakon" (probably a general term for heart disease). He recommended the application of astringent poultices to the precordium, measures (not specified) to prevent sweating, the ingestion of small quantities of food and wine at frequent intervals and the use of nutrient enemas if necessary. (See pages 14, 15.)

1649 Jean Riolan (Riolanus) (1577–1657), of Paris, was the first to advocate aspiration of the pericardium. He suggested trephining of the sternum as the approach to the pericardium. No record exists to the effect that Riolan practiced this procedure. (See pages 57, 58.)

Circa 1728 Hermann Boerhaave (1668–1738), of Leyden, refused to prescribe foxglove (digitalis), as he considered it a poison. (See pages 79, 80.)

1749 Jean-Baptiste de Sénac (1693–1770) of Versailles, used quinine in the treatment of "rebellious palpitations" (auricular fibrillation?). (See pages 81, 82.)

18th century John Fothergill (1712–1780), of Edinburgh and London, was aware of the relationship of flatulence to the precipitation of anginal seizures and advocated essence of peppermint to facilitate eructation of gas and mild laxatives to prevent constipation. He advised against the use of digitalis in disease of the aortic valve. (See pages 89, 90.)

1785 William Withering (1741–1799), of Stafford and Birmingham, introduced foxglove (digitalis) into general practice in the treatment of the failing heart and wisely defined its preparation, administration, contraindications and dangers. He was not certain as to the exact action of the drug but believed that it directly influenced the heart. (See pages 90, 91.)

1789 Caleb Hillier Parry (1755–1822), of Bath, advocated compressing the carotid artery in the treatment of nervous affections. He believed that this procedure diminished the blood flow to the brain and contended that the procedure benefited patients who had fits. Also by applying a tourniquet to the arteries of the limbs he stated that he observed improvement when certain diseases of the extremities existed. (See pages 95, 96.)

1814–1817 Friedrich Ludwig Kreysig (1770–1839), of Berlin, advocated the use of digitalis and called the drug a "God-given remedy." (See pages 113, 114.)

1831 James Hope (1801–1841), of Edinburgh and London, advised the restriction of fluid intake of patients exhibiting anasarca. (See pages 121, 122.)

1832	Sir Dominic John Corrigan (1802–1880), of Dublin, decried the use of digitalis in cases of aortic insufficiency. (See pages 122, 123.)
1835	Jean-Baptiste Bouillaud (1796–1881), of Angoulême and Paris, was a prodigious blood-letter and favored very rapid bleeding, which he referred to as "coup sur coup." He stated that digitalis was the "opium of the heart." (See pages 124, 125, 126.)
1st half of the 19th century	Joseph Skoda (1805–1881), of Pilsen and Vienna, is said to have been the originator of the so-called therapeutic nihilism which characterized this era of Viennese medicine. Actually he abandoned useless procedures such as bleeding and purgation after thorough clinical treatment. (See page 128.)
1st half of the 19th century	Johannes Evangelista Purkinje (1787–1869), of Breslau and Prague, described the visual manifestations of digitalis intoxication. (See page 129.)
1867	Sir Thomas Lauder Brunton (1844–1916), of Edinburgh and London, contributed the most important therapeutic innovation since Withering's classic publication on digitalis. Brunton introduced amyl nitrite for the relief of angina pectoris and discussed the action of the drug. (See pages 159, 160.)
1867	Richard Payne Cotton (1820–1877), of London, employed the following measures in his attempt to cause the cessation of paroxysmal tachycardia: antacids, stimulants of various kinds, aperients and conservative doses of digitalis. (See pages 160, 161.)
1874	Paul-Louis Duroziez (1826–1897), of Paris, was one of the first to call attention to the development of delirium during the administration of digitalis. (See pages 154, 155.)
1877	Reginald Southey (1835–1899), of London, introduced trocar-like tubes to be inserted into the tissues of edematous limbs in cases of anasarca to permit the escape of fluid. These cannulas became known as "Southey tubes" and are still mentioned in modern textbooks. (See page 181.)
1879	William Murrell (1853–1912), of London, introduced glyceryl trinitrate (nitroglycerin) in the treatment of angina pectoris. (See page 188.)
1895	S. Askanazy (1866–), of Germany, produced theobromine-sodium salicylate (diuretin), which was the forerunner of all the purine diuretics and vasodilator drugs. (See page 202.)
1901 and 1905	Harry Orville Hall, of Washington, D. C., recorded important observations dealing with the cerebral manifestations of digitalis intoxication. (See pages 224, 225.)
1908	Max Cloetta (1868–1940), of France, investigated the various fractions of the digitalis group and concluded that digitoxin was the most active fraction and produced all the effects of digitalis. In its water-soluble form, combined with digitonin, digitoxin was prepared under the trade name of "digalen." (See page 231.)

1914 Alfred Einstein Cohn (1879–), of New York, was apparently the first to describe the effect of digitalis on the T waves of the electrocardiogram. He inferred that the graphic changes resulted from an alteration in the contractile substance of the heart. (See pages 250, 251.)

1918 Karel Frederik Wenckebach (1864–1940), of Groningen and Vienna, in collaboration with Frey reported on the favorable effects obtained by the new drug quinidine in abolishing auricular fibrillation. (See pages 229, 230.)

1920 P. Saxl (1880–1932) and R. Heilig, of Germany, were the first to employ the double salt of sodium mercurichlorphenyloxyacetate with diethyl barbituric acid (novasurol) in the treatment of cardiac edema. This preparation was the forerunner of the modern mercurial diuretics. (See pages 254, 255.)

1925 Felix Mandl (1892–), of Germany, reported temporary arrest of the anginal seizures following the injection of procaine hydrochloride into the first five thoracic dorsal nerve roots. (See page 257.)

INDEX OF PERSONAL NAMES

(Names in italics are those of authors whose contributions are featured in this volume; numbers in italics refer to special biographies.)

GUIDE TO INDEX OF SUBJECTS

The subject index to this volume has been compiled with the aim of enabling the reader to retain the historical perspective and to appreciate the group relationships involved. For this purpose many of the more specific items have been included only under certain general headings. The following guide is designed to assist the reader in locating such items.

General Heading	*Class of Items Included*
Arrhythmia	Variations in heart rhythm
Art	Painting in relation to medicine
Biographic accounts	Special biographies of outstanding figures
Cardiac murmurs	All material on heart murmurs
Clinicopathologic correlations	Relations between clinical material and pathologic findings
Conduction system	The heart impulse and the structures concerned with it
Congenital anomalies of heart and great vessels	All congenital defects of the heart
Electrophysiology	The electrical activity of the heart and its measurement
Eras	Historical periods in relation to medicine
Inscription	Methods of recording medical findings
Instruments	Mechanical devices for measuring heart action or treating heart disease
Literature, medical	Medical journals
Magnification	Optics and the microscope
Papyrus	Papyri dealing with medicine
Physiology	Physiologic discoveries and theories
Remedies	Drugs and other methods of therapy
Schools	Medical sects and schools of thought
Signs	Eponymic diagnostic signs
Societies	Medical societies and academies

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